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This journal is planned to provide the reader with a selection of abstracts of the more important articles appearing in medical periodicals published in different parts of the world. Comment by the abstracter, when thought necessary, is inserted between square brackets, usually at the end of an abstract. In some instances only the titles of articles are provided.

The titles of journals are given in full and also abbreviated according to the rules adopted in the *World List of Scientific Periodicals* and in *World Medical Periodicals*. The titles of articles from foreign journals are translated into English.

This journal is essentially a guide to work in progress in the world's medical centres. No abstract can be regarded as a substitute for the article abstracted. For complete information the original article must be consulted. Our aim is to give the reader sufficient details in an abstract to enable him to judge whether the original is, for him, worth reading in full.

The abstracts are grouped in broad classifications and, so far as possible, those dealing with medical and surgical aspects of the same problem appear together under the same heading. The specialist will, it is hoped, learn from this journal of work done in other fields as well as in his own. The general practitioner will be able to keep abreast of modern knowledge in the various specialties. The representation in one journal of the several aspects of Medicine will, it is believed, give an integrated picture of the whole, necessary in this age of specialization.

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VOL. 15 NO. 2 FEBRUARY, 1954

Pathology

339. **Tubeless Gastric Analysis**
J. HARKNESS and J. A. DURANT. *Journal of Clinical Pathology* [*J. clin. Path.*] **6**, 178–182, Aug., 1953. 1 fig., 5 refs.

The technique introduced by Segal *et al.* (*Proc. Soc. exp. Biol.* (*N.Y.*), 1950, **74**, 218; *Abstracts of World Medicine*, 1950, **8**, 608) for detecting the presence or absence of gastric achlorhydria without intubation is based on the fact that free hydrogen ions in the gastric juice will displace quininium cations from a quininium-resin indicator (" diagnex ") at a *p*H of 3 or less. The quinine hydrochloride thus released appears in the urine within 15 minutes of ingestion of the resin and may be estimated quantitatively by comparing its fluorescence in ultraviolet light with that of standard solutions of quinine. The technique of the test as performed by the present authors is as follows. After an overnight fast the patient empties his bladder and the urine is discarded. He is then given 250 mg. of caffeine and sodium benzoate dissolved in water, 100 ml. of 7% alcohol, or a cup of tea or coffee without sugar or milk. About an hour later the bladder is emptied, the urine being saved as a control, and 2 g. of diagnex (36 mg. of quinine) is given suspended in water or alcohol (together with an injection of 0·5 mg. of histamine when required). After about one hour, and again after exactly 2 hours, the bladder is emptied, the urine specimens being collected in dark brown bottles, and the quinine content of all 3 samples determined. On the basis of their findings the authors consider that the excretion of 27 μg. of quinine or more in 2 hours indicates the presence of free hydrochloric acid in the stomach, while a figure of 23 μg. or less indicates achlorhydria. (The corresponding values given by Segal are 25 and 15 μg. respectively.) The test does not allow the amount of free acid in the gastric juice to be estimated quantitatively.

The results of this test were compared with those of the alcohol–histamine test meal in 180 subjects, some of whom were selected as likely to give anomalous results. In 115 cases the alcohol test meal showed free hydrochloric acid to be present; in 100 of these this finding was confirmed by the tubeless method without histamine, and in a further 8 on repeating the test with histamine. Of the 7 remaining cases, in 2 there was no opportunity to repeat the quinine test with histamine, in 3 cases failure to excrete quinine could be attributed to inadequate renal function, and in one case repeated alcohol test meals showed achlorhydria to be present intermittently; in one case only could the discrepancy not be explained. Of the 65 cases in which the alcohol test meal showed achlorhydria to be present, confirmation was obtained with the quinine test in 56; of the 9 discrepant results, one was due to a dose of diagnex having been given 2 days previously, and in 6 others to treatment with substances causing displacement of quinine from the resin (aluminium, calcium, barium, magnesium, kaolin, iron, or vitamins); in all these cases confirmation of the test-meal result was obtained on repeating the quinine test after the appropriate precautions had been taken. Of the 2 remaining cases, one could not be explained, but in the other the test meal had been performed without histamine, so that the finding of achlorhydria was suspect; both these patients had previously undergone partial gastrectomy.

The authors conclude that their results show the tubeless technique to be reliable, provided care is taken to exclude certain sources of error, and suggest that it may be most useful as a screening test in the detection of achlorhydria among patients suspected of having gastric carcinoma. *M. Lubran*

340. **Relationship of Alimentary Lipaemia to Blood Coagulability**
H. W. FULLERTON, W. J. A. DAVIE, and G. ANASTASOPOULOS. *British Medical Journal* [*Brit. med. J.*] **2**, 250–253, Aug. 1, 1953. 38 refs.

At the University of Aberdeen, the authors have investigated the influence of alimentary lipaemia on the accelerated clotting time (prothrombin time), using Russell-viper venom as the source of thromboplastin, and on the coagulation time estimated in silicone-coated tubes.

In 8 patients there was no significant change in the accelerated clotting time after a meal containing 12 to 30 g. of fat. In 5 patients an average reduction in the accelerated clotting time of 4·9 seconds was observed at the height of the lipaemia after a meal containing 65 g. of fat, while in 6 patients the average reduction was 9·8 seconds after a meal containing 85 g. of fat. A venom thromboplastin was selected because other thromboplastins already contain lipid, and the effect of alterations in plasma lipid content is thereby obscured.

The clotting time, measured in silicone-coated tubes, was estimated in 15 patients after a meal rich in fat (80 to 85 g.). In all patients with a post-prandial lipaemia the clotting time was reduced. The maximum lipaemia and effect on the coagulation time occurred about 3 hours after food. In 2 patients in whom lipaemia did not occur there was no significant reduction

in the clotting time. Control observations on 9 patients showed that after an ordinary hospital breakfast (12 to 30 g. of fat) there was a significant reduction in the clotting time in one; this was the only patient in the series with alimentary lipaemia.

The authors discuss the significance of the results in relation to thrombosis and to the development of atherosclerosis. *A. Brown*

EXPERIMENTAL PATHOLOGY

341. **Formation of Thromboplastin in Shed Mammalian Blood**
P. Fantyl and R. A. Hayes. *Nature* [*Nature (Lond.)*] **172**, 303–304, Aug. 15, 1953. 1 fig., 7 refs.

The authors present briefly the results of an investigation carried out at the Medical Research Institute, Melbourne, into the reason for the accelerated clotting time, that is, the reduced coagulation time, obtained with citrated whole blood. The results, which are shown on a graph, are regarded as supporting the belief that normal blood plasma contains a soluble precursor of the thromboplastin complex which becomes activated when in contact with glass, the latter most probably acting as a kinase. In silicone-coated tubes there was an initial fall in the coagulation time, but little further change during the period of incubation (15 minutes). *A. Brown*

342. **Erythrocytosis-promoting Activity in Stagnant Blood and in Blood Subjected to Low Atmospheric Pressure *in vitro*.** [In English]
E. Hirsjarvi. *Annales medicinae experimentalis et biologiae Fenniae* [*Ann. Med. exp. Biol. Fenn.*] **31**, Suppl. 3, 1–77, 1953. 6 figs., bibliography.

343. **The Problem of Formation of an Artificial Collateral Circulation.** (Проблема создания искусственного окольного кровообращения)
B. P. Kirillov. *Хирургия* [*Khirurgiya*] 3–13, No. 2, Feb., 1953. 8 figs.

In a series of experiments on dogs the author and co-workers have explored the possibility of creating an artificial collateral circulation which would be adequate to maintain the normal function of an organ after ligation of the vessels normally responsible for its blood supply.

In one dog the left kidney was stripped of its capsule and wrapped in omentum. Some 4 weeks later the left renal vessels were tied and divided, and after another interval of 4 weeks the right kidney was removed. This dog has survived for 8 months so far, although it has only one kidney, which is dependent for its blood supply on omental vessels. In another experiment a band of omentum was wrapped around the vessels of the lower limb and buried under the skin; 4 weeks later both common iliac arteries were ligated. In the limb with the omental graft there was a transient paresis, but in the opposite limb a permanent paralysis developed.

The author concludes that in the dog it is practicable to bridge the site of obstruction in a large vessel by omental grafting. *Z. W. Skomoroch*

344. **Microscopic Observations of the Pulmonary Arterioles, Capillaries, and Venules of Living Mammals before and during Anaphylaxis**
W. S. Burrage and J. W. Irwin. *Journal of Allergy* [*J. Allergy*] **24**, 289–296, July, 1953. 7 figs., 11 refs.

Changes in the pulmonary arterioles, capillaries, and venules of guinea-pigs and rabbits during anaphylaxis were studied microscopically at Harvard Medical School. A small part of the lung surface was exteriorized after respiratory movements had been abolished by insufflation of oxygen through a tracheotomy opening. In anaphylactic shock a marked contraction of the pulmonary arterioles was observed, followed by a stoppage of the linear blood flow in the capillaries. During this time the heart was still beating vigorously, but the animal rapidly became cyanotic and died within 2 to 4 minutes. In some animals these changes were not so marked; the blood flow continued, and leucocytes were found adhering to the walls of the arterioles. Small emboli were seen and some clumping of erythrocytes (" sludging ") occurred. These animals died within 10 to 20 minutes of the anaphylactic shock. In a very few animals the changes were reversed and normal circulation was restored. *H. Herxheimer*

345. **The Nervous System and Acute Pulmonary Oedema.** (Нервная система и острый отек легких)
G. S. Kan. *Вестник Хирургии* [*Vestn. Khir.*] **73**, 20–24, May–June, 1953.

The author has studied the relationship between the nervous system and pulmonary oedema in rabbits and cats. The rabbits were given 0·6 mg. of adrenaline per kg. body weight into the marginal vein of the ear; the cats were subjected to rapid intra-arterial injections of normal saline in quantities 1½ to 2½ times their total blood volume. In the rabbits cervical vagotomy was found to prevent the pulmonary oedema caused by adrenaline. Sub-threshold doses of adrenaline, however, when given simultaneously with the electrical stimulation of the central end of the divided vagus nerve, produced acute oedema.

In the cats the rapid intra-arterial infusion of normal saline led to acute pulmonary oedema. The same quantity of normal saline, however, given intravenously and slowly, was well tolerated; but if at the same time the splanchnic nerves or those supplying the aorta or carotid sinus were stimulated, pulmonary oedema developed. Further, the exclusion of the sympathetic nervous system by drug block or by section of the spinal cord prevented the appearance of pulmonary oedema, but section of the brain at the level of the corpora quadrigemina had not this effect.

On the basis of these results the author believes that pulmonary oedema is a pathological reflex produced by stimuli coming from widespread " receptor zones " in the lungs, passing through the brain-stem below the corpora quadrigemina, and having efferent pathways in the sympathetic nerves. He suggests that the phenomenon represents a physiological defence mechanism which acts by elimination of surplus body water through the lungs. *Z. W. Skomoroch*

346. **Changes in the Loose Connective Tissue during Sensitization.** (Изменения рыхлой соединительной ткани при сенсибилизации)
A. M. VIKHERT. *Архив Патологии* [*Arkh. Patol.*] **15**, 30–36, July–Aug., 1953. 4 figs., 12 refs.

This study of the changes occurring in loose connective tissue during sensitization was carried out on 31 rabbits divided into 11 groups according to the number of injections of antigen given. An allergic state was induced by the subcutaneous injection of 1 ml. of horse serum, the number of injections varying from one to 10, given at 3-day intervals; the 11th group received "about 30 injections", in doses of 0·5 ml. The animals were killed 5 days after the last injection. Repeated skin biopsies from various parts of the body were taken during the experiment.

Histological changes in the cells of loose subcutaneous tissues were observed even after the first injection, and were as follows. An increase in the number of histiocytes, partly due to amitotic division of the existing histiocytes and partly a result of differentiation of adventitial cells situated along the arterioles and capillaries (the "adventitial histiocytes" of Jasvoin). The author also mentions some narrow, elongated cells, poor in protoplasm, which constituted a third source of histiocytes. The number of histiocytes increased up to the time of the 4th or 5th injection, but thereafter remained constant. In about one-third of the animals this reaction was very weak. In the majority of cases the phenomenon was also accompanied by an increase in the numbers of "polyblasts".

Morphological changes were also observed in histiocytes and fibroblasts. Both types of cell showed vacuolation of the cytoplasm, which increased with the number of injections. The fibroblasts also tended to lose their ectoplasm and cytoplasmic processes and to become rounded. The author regards vacuolation as a sign of an increased activity of the cells in connective tissue. He argues that all these cells should be considered as a single functional system, and that the term reticuloendothelial system should be abandoned. *A. Swan*

347. **Temporal and Quantitative Factors Influencing the Development of Experimental Asthma in the Guinea Pig**
B. RATNER. *Journal of Allergy* [*J. Allergy*] **24**, 316–325, July, 1953. 9 refs.

[In this paper earlier work by the author on experimental asthma (*Amer. J. Dis. Child.*, 1939, **58**, 699–733) is again reported and the same seven tables are reproduced, but the earlier publication is not quoted in the list of references or referred to otherwise.] In the original experiments it was shown that when guinea-pigs were exposed to the inhalation of finely-dispersed horse dander, sensitization occurred with greater frequency as the total period of exposure was increased. The author's interpretation of his results differs from that originally given in some respects—for example, the failure of certain animals originally strongly sensitized to react to further exposures is now attributed to desensitization rather than to other factors—and the conclusion is now drawn from these findings that in spite of individual differences in susceptibility to sensitization, almost every animal can be sensitized if it is exposed to the antigen for a sufficient length of time. *H. Herxheimer*

348. **The Effect of Stress Factors on Asthma Induced in Guinea Pigs by Aerosolized Antigens**
S. M. FEINBERG, S. MALKIEL, and F. C. MCINTIRE. *Journal of Allergy* [*J. Allergy*] **24**, 302–308, July, 1953. 14 refs.

An investigation was carried out at the Northwestern University, Chicago, to determine the effect of certain stress factors on asthma induced in guinea-pigs passively sensitized to egg albumen and exposed to an antigen aerosol. The period of exposure required to produce cough or dyspnoea was used as a measure of the degree of the sensitization achieved. It was found that when 50 mg. of cortisone was injected 18 hours before exposure to the antigen the exposure time was more than double that tolerated by control animals not receiving cortisone. This partial protection was also observed when 10 mg. of ACTH was injected 8 and 4 hours before exposure. Significant protection was also achieved when the animals were given a subcutaneous injection of dried yeast, but heated yeast or yeast extract had little effect.

[The dose of 50 mg. of cortisone per animal (approximately 100 mg. per kg.) is so high that the results do not bear comparison with those obtained by other workers in the same field.] *H. Herxheimer*

MORBID ANATOMY AND CYTOLOGY

349. **Primary Carcinoma of the Pituitary**
E. H. FEIRING, L. M. DAVIDOFF, and H. M. ZIMMERMAN. *Journal of Neuropathology and Experimental Neurology* [*J. Neuropath.*] **12**, 205–223, July, 1953. 11 figs., 28 refs.

The clinical and pathological findings in 3 cases of primary carcinoma occurring in a series of 77 verified cases of pituitary tumour are described and compared with those in similar cases recorded in the literature. The ages of the patients at the time of the onset of symptoms were 21, 31, and 47 years respectively, and the total duration of the illness was about 6 years in each case. The clinical manifestations were not distinctive, except in one case in which Cushing's syndrome developed relatively late and after the second of two operations. Visual disturbances and the involvement sooner or later of the facial and acoustic nerves occurred in every case and oculomotor and abducens involvement in one, but in none was the trigeminal nerve involved. The final clinical picture was thus a combination of the syndromes characteristic of tumours of the middle fossa and cerebello-pontine angle.

In the absence of biopsy material, recognition of the malignant nature of such tumours is very difficult. Radiography of the skull provided no clue in the authors' cases and, although the tumour was of large size in each case, this alone cannot be accepted as an indication of malignancy in a pituitary tumour. But since irradiation is usually effective in the treatment of benign pituitary neoplasms, failure to respond should certainly suggest

malignancy; in none of these cases was sustained relief afforded by irradiation. Surgical treatment gave temporary relief in one case but failed completely in the remaining 2.

The histological appearance of the tumour in the authors' cases was entirely different from that of a chromophobe adenoma. Specific cell granules were absent, and instead of the alveolar arrangement of cells characteristic of an adenoma, the neoplastic tissue consisted of sheets of cells of varying size and shape, multinucleated cells and mitotic figures being present in large numbers. Metastatic deposits were observed in the anterior fossa in one case, but no extracranial deposits were seen. In one case the tumour appeared to be mixed, the cells being carcinomatous at the periphery and sarcomatous at the centre. *Adrian V. Adams*

350. **Tumours of the Thymus. New Data and an Attempt at Classification.** (Les tumeurs du thymus. Données nouvelles, tentative de classification)
C. OBERLING. *Bulletin de l'Association française pour l'étude du cancer* [*Bull. Ass. franç. Cancer*] **40**, 139–169, 1953. 23 figs., 44 refs.

The author presents, from the Gustave-Roussy Institute for Cancer Research, Paris, 8 cases of tumour of the thymus (collected from various sources), and discusses modern ideas of their classification, which, as he states, have been much modified by the number of asymptomatic cases revealed by routine *x*-ray examination. He divides the group into (1) epitheliomata [in the correct French fashion, tumours of epithelium], (2) thymomata (or, more helpfully, thymocytomata), and (3) pseudogranulomatous epitheliomata (the Hodgkin-like thymomata described by Lowenhaupt). The epitheliomata can be further subdivided into embryonic and adult types; they have a long phase of encapsulation followed by rapid dissemination, and are only occasionally accompanied by myasthenia. The thymomata are purely thymocytic, are usually benign, and are accompanied by myasthenia more often than are the epitheliomata. The pseudogranulomatous epithelioma progresses like a reticulosis, and does not produce myasthenia. Of the 8 tumours described (mostly in detail and with excellent photomicrographic illustrations) 4 were in the first category, 2 in the second, and 2 in the third. Support is afforded to the view that thymocytes of the normal thymus are of dual origin, partly from thymic epithelium and partly true lymphocytes. *Bernard Lennox*

351. **Pathology of Primary and Recurrent Carcinoma of the Human Breast after Administration of Steroid Hormones**
W. J. EMERSON, B. J. KENNEDY, J. N. GRAHAM, and I. T. NATHANSON. *Cancer* [*Cancer (N.Y.)*] **6**, 641–670, July, 1953. 44 figs., 22 refs.

The authors give an account of the regressive changes occurring in 18 cases of primary and 46 cases of recurrent carcinoma of the breast after the administration of oestrogens, usually stilboestrol in a daily dose of 15 mg. Mastectomy was performed 3 to 19 months after hormone therapy was started, tumour tissue removed before and after operation being examined microscopically. Control material consisted of tissue from 110 consecutive cases of carcinoma treated by mastectomy alone.

In the hormone-treated patients there was a variable degree of degeneration of tumour cells, with loosening of the surrounding fibrous stroma. Later there was much scarring of the tumour area. Similar changes, but far less marked, were seen in the control series. Regression tended to be more pronounced in the more slowly growing tumours. *A. Wynn Williams*

352. **Significance of Gastric Polyps Accompanying Cancer**
R. G. MCMANUS and S. C. SOMMERS. *American Journal of Clinical Pathology* [*Amer. J. clin. Path.*] **23**, 746–757, Aug., 1953. 12 figs., 18 refs.

With the object of ascertaining the relation, if any, of gastric polyp to carcinoma, the authors studied the history and pathological findings in 45 cases of gastric polyp seen at the Pondville Hospital, Walpole, and the New England Deaconess Hospital, Boston, Mass. In 20 cases the polyps were multiple. In 34 of the 45 cases (75%) there were malignant growths, the total number of tumours being 53. The authors state that this high figure was not unexpected, since the cases were drawn from institutions in which the incidence of carcinoma at necropsy was high. The most common site of the carcinoma was the gastro-intestinal tract (25 tumours), followed by the endocrine-stimulated organs (17 tumours); the remaining 11 carcinomata were found in miscellaneous sites. There was some overlap as between the first two groups, there being 13 cases in the series in which there was more than one primary growth.

The authors suggest that gastric polyps, like endometrial polyps, are partly dependent on hormonal imbalance for their development—a suggestion which receives support in this series from the fact that the endocrine organs and their responsive end-organs showed nodular hyperplastic overgrowth. Metabolic disturbances, such as obesity, hypertension, and diabetes mellitus, were also found, while in 7 out of 10 pituitary glands examined morphological changes believed to indicate hyperfunction were observed. *J. B. Wilson*

533. **Pontine Hemorrhage in Intracranial Hypertension**
W. S. FIELDS and B. HALPERT. *American Journal of Pathology* [*Amer. J. Path.*] **29**, 677–687, July–Aug., 1953. 4 figs., 5 refs.

The brains of 43 patients who had had raised intracranial pressure during life were examined at Baylor University, Houston, Texas, to determine the frequency of pontine haemorrhage. The "intracranial hypertension" (as the authors term increased intracranial pressure) was due to intracranial haemorrhage in 20 patients, primary neoplasm in 14, metastatic deposits in 8, and brain abscess in one. Extensive haemorrhage into the pons or midbrain was found in 11 of the 20 patients who had had an intracranial haemorrhage, in 5 of those with a primary neoplasm, and in the patient with a cerebral abscess. No haemorrhage was observed in the patients with metastatic deposits in the brain.

The mechanism which produced this haemorrhage into the pons is discussed, and from an analysis of the clinical findings the authors conclude that such haemorrhage occurs only in those patients in whom there is a sudden change in intracranial hydrodynamics—that is, a sudden change in intracranial pressure. This change may be initiated by trauma, lumbar puncture, ventriculography, or craniotomy. From their observations the authors believe that herniation through the tentorial incisura is a more frequent cause of a sudden change in intracranial pressure than is herniation of the cerebellum and medulla through the foramen magnum.

[The article is accompanied by a number of excellent illustrations.] *Ruby O. Stern*

354. **Coronary Embolism in Bacterial Endocarditis**
J. G. BRUNSON. *American Journal of Pathology* [*Amer. J. Path.*] **29**, 689–701, July–Aug., 1953. 8 figs., 16 refs.

In 7 out of 9 successive cases of bacterial endocarditis examined post mortem in the Department of Pathology of the University of Minnesota emboli were found in the coronary arteries, being multiple in 4 cases. Changes in the myocardium were found in all cases, taking the form of ischaemic necrosis in various stages of organization, abscess formation, or calcified areas which were regarded as healed abscesses. The coronary arteries showed no evidence of atheroma, and the material in the lumina of the blocked vessels was similar to that on the affected valves.

The author concludes that coronary embolism is of common occurrence in bacterial endocarditis and suggests that this is due to the location of the orifices of the coronary arteries, the mechanics of the blood flow past them, and the manner of opening of the aortic valve cusps. *R. H. Heptinstall*

355. **The Pathogenesis of the Rheumatic Granuloma.** (Zur Pathogenese des rheumatischen Granuloms)
A. VON ALBERTINI. *Schweizerische medizinische Wochenschrift* [*Schweiz. med. Wschr.*] **83**, 772–776, Aug. 22, 1953. 6 figs., 31 refs.

On the basis of observations made at the Institute of Histopathology, University of Zürich, the author considers that the primary lesion in the Aschoff body in rheumatic myocarditis is tissue necrosis, and that this necrosis may occur not only in connective tissue, but also in muscle fibres. The cellular reaction which develops for the reabsorption of these necroses consists mainly of basophil histiocytes, which may be converted into Anitschkow cells. These Anitschkow cells are not myocytes—for besides being seen in the myocardium they also occur in the endocardium and epicardium—but are the form taken by basophil histiocytes in the heart (to which Anitschkow cells appear to be limited) in rheumatism and endocarditis lenta, and in the healing of experimental wounds of the heart and of cardiac infarcts.

The structure of the granuloma, however, provides no evidence regarding its cause, but it is suggested that streptococcal infections and associated allergic factors may be responsible. *C. L. Oakley*

356. **Rheumatic " Activity " as Judged by the Presence of Aschoff Bodies in Auricular Appendages of Patients with Mitral Stenosis. 1. Anatomic Aspects**
J. P. DECKER, C. VAN Z. HAWN, and S. L. ROBBINS. *Circulation* [*Circulation (N.Y.)*] **8**, 161–169, Aug., 1953. 6 figs., 28 refs.

Histological study at the Peter Bent Brigham and Boston City Hospitals of 183 auricular appendages, out of a total of 223 removed at operation from patients thought to be free of active carditis, showed the presence of Aschoff bodies in 83 (45%), these bodies being numerous (up to 10 or 12) in 21 cases (11·5%). They were located in the endocardium or, more commonly, in the loose-structured subendocardium; none were in the myocardium proper. Of 172 appendages examined, endocardial thrombosis was present in 71 (41%), but in these cases the incidence of Aschoff bodies was low. In 6 of the 22 cases coming to necropsy and showing Aschoff bodies it was found that when these lesions were frequent in the left auricular appendage, they were also frequent in the left ventricular myocardium, and vice versa.
A. C. Lendrum

357. **On the Effect of the Hyaline Membranes in the Lungs of Newborn Infants.** [In English]
S. RANSTRÖM. *Acta paediatrica* [*Acta paediat. (Uppsala)*] **42**, 323–329, July, 1953. 2 figs., 10 refs.

In 30 cases of hyaline membrane of the lungs in newborn infants examined by the author in the Department of Pathology of the University of Uppsala, the effects, rather than the mode of formation, of the membranes were studied. As a result it is suggested that in many instances these membranes are of no functional significance, death being due to some other condition. The author draws attention to the importance of distinguishing between primary (or residual foetal) atelectasis and secondary atelectasis. In the former type membrane may block the last areas of lung available for oxygen absorption, but is not responsible for the atelectasis, which is the primary cause of death. In most cases of the latter type the hyaline membrane found is insufficient to account for more than a small proportion of the collapsed lung tissue and, in the author's opinion, membrane formation is an important factor in the causation of secondary atelectasis only when the membranes are very abundant and widespread. *G. J. Cunningham*

358. **The Basic Lesion in Chronic Pulmonary Emphysema**
D. M. SPAIN and G. KAUFMAN. *American Review of Tuberculosis* [*Amer. Rev. Tuberc.*] **68**, 24–30, July, 1953. 9 figs., 5 refs.

The authors reiterate the original observations of Laënnec and of Rokitansky that the basic lesion of chronic pulmonary emphysema is the presence of obstructive lesions in the terminal bronchioles, and not a primary change in the alveolar walls as has been suggested by other workers. In the study here reported from Grasslands Hospital, Valhalla, New York, they examined lungs obtained post mortem from 10 men over the age of 50 who during life had all suffered from chronic

pulmonary emphysema, but in none of whom had there been asthma, bronchiectasis, or any other condition which might produce obstructive lesions. Controls were provided by examining lungs from male subjects of the same age group who had died from non-pulmonary disease and who had given no evidence of emphysema during life.

Histological examination showed that whereas the terminal bronchioles in the emphysematous lungs were identified without difficulty, this was not so in the normal lungs. Also in emphysematous lungs the terminal bronchioles showed chronic inflammatory changes with hypertrophy of the musculature, a longer and more tortuous course, varying degrees of pulmonary arteriolar sclerosis, and there was usually stenosis of the lumen. These changes were diffuse, and occurred most characteristically in bronchioles less than 0·35 mm. in diameter. The authors conclude that while it may be assumed that the alveolar changes could readily be explained as a development consequent on the obstructive lesions, the assumption that the primary lesion is an alveolar change would be insufficient to explain the changes in the bronchiolar tree. *E. G. Rees*

359. **Ulcero-caseous Tuberculous Bronchitis. A Method of " Spread " in Pulmonary Tuberculosis**
J. W. CLEGG. *Thorax* [*Thorax*] **8**, 167–179, Sept., 1953. 20 figs., 1 ref.

The thesis is developed that ulcerocaseous tuberculous bronchitis arises in isolated small bronchial segments as the initial tuberculous lesion in areas of lung tissue previously normal.

Lung specimens are described and illustrated in which there were small lesions in the bronchi but no pneumonic process was found in the surrounding tissues. The earlier stages of this caseous tuberculous bronchitis are easily overlooked in histological sections when only the smaller bronchi and bronchioles are involved, especially if these are seen only in cross-section. These lesions are too small to be recognized on a radiograph.

When the entire bronchial tree of a segment is involved there is a marked degree of collapse, so that the ulcerocaseous process can readily spread through the collapsed lung, the caseous and expanded bronchi fusing and becoming confluent. In this way a " bronchial cold abscess " is formed, which is large enough to be detected in the radiograph. Abscesses of this type may be single, giving rise to solitary caseous foci, or they may be multiple, giving rise to disseminated caseous foci.

It is pointed out that it is often very difficult to determine whether a fully developed caseous lesion has in fact arisen as a result of ulcerocaseous bronchitis or from an area of tuberculous pneumonia. If a thorough examination is made, however, such bronchial remnants as cartilage, mucous gland, or epithelium can usually be found when the lesion is a consequence of ulcerocaseous bronchitis. Furthermore, in true pneumonic lesions elastic tissue can usually be demonstrated outlining the remnants of alveolar walls destroyed in the expanded state. In the bronchogenic cold abscess the alveoli are collapsed.

The bronchial cold abscess may heal either by fibrosis or by calcification, either process leading to bronchial stenosis. *R. B. Lucas*

360. **A Comparative Study of the Vascular Supply of Tuberculous Cavities and of Circumscribed Caseous Foci.** (Étude comparée de la vascularisation des cavernes tuberculeuses et des foyers caséeux circonscrits)
J. DELARUE, C. SORS, and J. MIGNOT. *Revue de la tuberculose* [*Rev. Tuberc. (Paris)*] **17**, 609–640, 1953. 22 figs., bibliography.

The blood supply of tuberculous cavities and of tuberculomata has been studied and compared by the authors by the radiographic and histological examination of lungs whose arteries have been injected with a 3% gelatin solution to which has been added 50% by weight of red lead. By this technique they claim to have demonstrated (1) that the region around a tuberculous cavity is supplied by an extremely rich vascular network mainly derived from the bronchial arteries; the thrombosed pulmonary arteries are partly recanalized and the vascular network is largely supplied by anastomoses between the bronchial arteries and the new lumen of the pulmonary arteries (intravascular anastomoses); (2) that the vascular network around a tuberculoma is much less rich, is somewhat farther away from the margin of the affected area, and is supplied by both pulmonary and bronchial arteries, between which the anastomoses (which are mainly intervascular in character) are fewer than those occurring around cavities; and (3) that obliteration of the pulmonary artery and subsequent intravascular anastomosis between bronchial and pulmonary arteries occur only near the liquefying parts of a tuberculoma. *C. L. Oakley*

361. **The Value of Liver Biopsy in the Diagnosis of Tuberculosis and Sarcoidosis**
E. S. FINCKH, S. J. BAKER, and M. M. P. RYAN. *Medical Journal of Australia* [*Med. J. Aust.*] **2**, 369–374, Sept. 5, 1953. 5 figs., 16 refs.

Needle biopsy of the liver has become an accepted procedure in the diagnosis and investigation of liver disease. In this paper from the Clinical Research Unit of the Walter and Eliza Hall Institute, Melbourne, the authors describe the results of liver biopsy in 7 cases of pyrexia of unknown origin and in 9 cases of obscure chest lesions. In 8 of these 16 cases granulomata histologically resembling those of tuberculosis or sarcoidosis were found, and unfixed material obtained at the same time or by a subsequent puncture was injected into guinea-pigs. In only one case was a positive result obtained, while acid-fast bacilli were demonstrated histologically only in this and one other case, although in 3 of the remaining cases the combination of clinical picture, histological appearances, and subsequent course enabled the diagnosis of tuberculosis to be made. This confirms the finding of other workers that the miliary type of tuberculous lesion encountered in the liver contains few viable tubercle bacilli. In the 8 cases in which the liver biopsy revealed no abnormality the condition was still undiagnosed when the patients were discharged.

The authors conclude that " liver biopsy followed by histological and bacteriological examination is a useful additional method of investigation of patients with pyrexias of unknown origin or obscure radiological lesions of the lungs, when other methods have failed to establish a diagnosis ". *E. Forrai*

362. **Needle Biopsy of the Kidney.** (La biopsie du rein à l'aiguille)
M. PAYET, P. PENE, R. CAMAIN, A. GOUAZE, and F. CALVEZ. *Presse médicale* [*Presse méd.*] **61**, 989–992, July 8, 1953. 6 figs., 18 refs.

An accidental puncture of the kidney without subsequent ill effects during needle biopsy of the liver and the excellent quality of histological preparations of the renal tissue thus obtained led the authors to consider the feasibility of renal biopsy as a planned procedure. Following a careful study on the cadaver, they developed, at the Dakar School of Medicine, a technique of which they now give details, by which the kidney is punctured from the loin, employing the same trocar (9 cm. long, external diameter 18 mm.) as for liver biopsy, attached to a 30- or 50-ml. syringe. The operation is preceded by excretion urography to exclude anatomical abnormalities of the kidney, and the puncture is made at the level of the first lumbar vertebral spine, one fingerbreadth outside the lateral border of the sacrospinalis muscle. The method has now been used in 55 cases of various renal conditions and has been wholly successful in 35. There has been no serious complication, though slight haematuria and localized perirenal haematoma have occurred. It is suggested that the technique may be useful in the differential diagnosis of certain renal diseases. The difficulty of the procedure is [wisely] emphasized and the contraindications and method of selection of cases are discussed. *G. J. Cunningham*

363. **Nephrosclerosis and the Glomerulus**
D. B. JONES. *American Journal of Pathology* [*Amer. J. Path.*] **29**, 619–631, July–Aug., 1953. 12 figs., 15 refs.

The author, working at the State University of New York, has extended his studies of renal glomeruli in sections 2μ thick stained to differentiate between the epithelial and capillary basement membranes (*Amer. J. Path.*, 1953, **29**, 33; *Abstracts of World Medicine*, 1953, **14**, 270) to include numerous cases of benign nephrosclerosis with or without diabetes, 23 of malignant hypertension, and 5 of diabetic glomerulosclerosis.

In benign nephrosclerosis he confirms the occurrence of hyaline arteriosclerosis and describes the interstitial accumulation of connective-tissue cells in the glomerulus as a primary change corresponding to the intimal connective-tissue proliferation of arteriolar sclerosis. Secondary changes in the glomeruli consist on the one hand in compensatory hypertrophy of a few units, and on the other to widespread ischaemic collapse due to simple loss of blood flow. The author considers that diabetic glomerulosclerosis represents the end-stage of a slowly progressive primary glomerular arteriolosclerosis.

In malignant nephrosclerosis he distinguishes inflammatory, reparative, and secondary changes. The first of these include fibrinoid arteriolar necrosis (present in 19 of his 23 cases), occasionally aneurysmal dilatation, thrombosis (9 cases), interstitial haemorrhage (5 cases), focal lobular oedema, and an inflammatory cellular exudate (6 cases). Exudative arteritis is stated to be rare. The reparative changes include capsular proliferation (6 cases), glomerular scarring due either to the secondary changes of benign nephrosclerosis or the healing of inflammatory changes, and occasionally hyperplasia of the juxta-glomerular apparatus. The secondary changes are similar to those observed in benign nephrosclerosis, with the addition of interstitial collections of lipophages.

[Fibrinoid necrosis, aneurysmal dilatation, thrombosis, interstitial haemorrhage, and focal lobular oedema are not usually regarded as evidence of glomerular inflammation in malignant nephrosclerosis. The absence of fibrinoid necrosis from the glomeruli in 4 of the 23 cases of malignant nephrosclerosis suggests that the diagnosis in these cases may have rested largely on clinical evidence.] *J. B. Entricknap*

364. **A Morphologic Study of the Myenteric Plexus and Musculature of the Pylorus with Special Reference to the Changes in Hypertrophic Pyloric Stenosis**
H. H. BELDING and J. W. KERNOHAN. *Surgery, Gynecology and Obstetrics* [*Surg. Gynec. Obstet.*] **97**, 322–334, Sept., 1953. 7 figs., 32 refs.

The distribution of the myenteric plexuses in the stomach of 15 healthy subjects and 14 patients with hypertrophic pyloric stenosis was studied at the Mayo Foundation, both adult and infant stomachs being examined.

Representative blocks of tissue were fixed in formalin, and paraffin sections stained with haematoxylin and eosin or cresyl violet, or by Bielschowsky's silver impregnation method (described by Mallory). The number of myenteric ganglion cells and nerve fibres per unit area was found to be reduced in the pylorus in hypertrophic pyloric stenosis, but was normal elsewhere in the stomach and also in the duodenum. Moreover, most of the ganglion cells in the pylorus were degenerate, resembling those seen after excessive stimulation of the vagus nerve.
A. Wynn Williams

365. **The Myenteric Plexus in Chronic Ulcerative Colitis**
K. A. STORSTEEN, J. W. KERNOHAN, and J. A. BARGEN. *Surgery, Gynecology and Obstetrics* [*Surg. Gynec. Obstet.*] **97**, 335–343, Sept., 1953. 5 figs., 13 refs.

At the Mayo Clinic the myenteric plexus in the colon of 25 patients suffering from ulcerative colitis was examined histologically with special reference to the number of ganglion cells, and the findings compared with those obtained on histological examination of the normal colon. The tissues were fixed in formalin and embedded in paraffin; all sections were stained with haematoxylin and eosin and with cresyl violet. An absolute increase in the number of ganglion cells in ulcerative colitis was observed, but the cause of the increase is not known.
A. Wynn Williams

Bacteriology

366. **Blood Mediums for Cultivation of *Mycobacterium tuberculosis*. V. Results with Agar-agar Basal Medium and Varying Concentrations of Blood, Glycerine and Penicillin**

M. S. TARSHIS. *American Journal of Clinical Pathology* [*Amer. J. clin. Path.*] **23**, 661–670, July, 1953. 3 figs., 19 refs.

Previous investigations into the use of a blood-containing medium for the culture of *Mycobacterium tuberculosis* showed that out-dated human bank blood (about 4 weeks old) can be used to advantage in a simple agar-agar base. After studying the effect of varying the proportions of the ingredients used, the author now recommends a medium of the following composition: agar-agar 1·5 g., glycerin 1 ml., human bank blood 30 ml., and water 69 ml., to which is added 50 to 100 units of penicillin per ml. The agar is dissolved in glycerin-water by heating, and sterilized for 15 minutes at a pressure of 15 lb. per sq. inch (1·05 kg. per sq. cm.), after which it is cooled to 45° C. in a water bath. Blood and penicillin solution are then added, the ingredients are thoroughly mixed, and the medium is dispensed aseptically in 3·5-ml. amounts into screw-capped bottles and allowed to harden in slants. When stored in the refrigerator the medium will keep for at least 4 months. Comparison with four different conventional egg media showed that the new blood medium was at least equal, and in some cases superior, to the others for the culture of sputum or the subculture of a known and virulent strain of *Myco. tuberculosis*, in regard to both early detection and final degree of growth. *R. Salm*

367. **Human Plasma and Blood Agar for Cultivation of Tubercle Bacilli**

M. E. CLARK. *American Journal of Clinical Pathology* [*Amer. J. clin. Path.*] **23**, 671–675, July, 1953. 9 refs.

In the laboratories of the New York State Department of Health, Albany, the author studied the suitability of blood- or plasma-containing media for the culture of tubercle bacilli. To beef-heart-infusion agar out-dated stored human blood or plasma was added in a concentration of 25%, and in some experiments a varying proportion of malachite green was also added. It was found that in plasma the dye exerts a definite inhibitory action on the growth of tubercle bacilli in a concentration of 0·025%, while in lower concentrations the number of contaminated slopes increased. But in the media containing whole blood the dye appeared to exert no action, growth of *Mycobacterium tuberculosis* being vigorous and comparing well with that on Loewenstein–Jensen egg medium, though it was perhaps not quite so heavy. The author recommends the use of whole-blood agar with or without malachite green for the cultivation of tubercle bacilli in small laboratories in place of egg media, which are more difficult to prepare. *R. Salm*

368. **Effect of Some Serums on Titer of Rh Antibodies. A Method for Detection of Rh Sensitization**

E. P. LEROY and W. SPURRIER. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **42**, 85–91, July, 1953. 1 fig., 17 refs.

The sera of 6 Rh-negative women who had been delivered of erythroblastotic infants were examined at the Mount Sinai Hospital, Chicago, for Rh antibodies by all known techniques, but none were detected. These sera were then used as diluents in the titration of known anti-Rh sera and the results compared with those obtained when pooled AB serum containing no Rh antibodies was used. The use of the former sera resulted in a significant enhancement of the titre obtained with the control AB serum, the enhancement being abolished by absorption with Rh-positive cells but not with Rh-negative cells. The presence of Rh antibodies in the sera of these 6 women was thus demonstrated although the standard tests had failed to detect them, and it is suggested that this method provides a more sensitive test for Rh sensitization than any technique hitherto available. *I. Dunsford*

369. **Tuberculosis and Leprosy: Immunological Studies in Healthy Persons**

J. LOWE and F. MCNULTY. *British Medical Journal* [*Brit. med. J.*] **2**, 579–584, Sept. 12, 1953. 33 refs.

A series of parallel tuberculin and lepromin tests were carried out in healthy Africans (81 children aged 1 to 15 years and 278 adults) in the Uzuakoli district of Nigeria. In both children and adults a statistically significant degree of association was found between the two sets of results; it is therefore concluded that both tests are modified by some common factor. The authors' observations are held to "afford strong evidence that exposure to tuberculous infection, as shown by a positive tuberculin test, can, and usually does, cause the lepromin test to become positive; in fact, the observations can be reasonably explained only on this basis; no other hypothesis appears able to explain the facts".

This conclusion receives support from the finding by the authors as well as earlier workers that the reaction to the lepromin test becomes positive in initially negative reactors after vaccination with B.C.G. Of 65 tuberculin-negative adults and children who received B.C.G. vaccine, 64 became tuberculin-positive. Before vaccination with B.C.G. 58 of the 65 were lepromin-negative; after vaccination 40 gave a positive and 14 a doubtful reaction to the lepromin test.

Since a positive reaction to the lepromin test is widely believed to indicate an increased resistance to leprosy, it is suggested that in countries in which this disease is endemic prophylaxis might be attempted by B.C.G. vaccination of those exposed to infection with leprosy, especially children. *G. Payling Wright*

Pharmacology

370. **Parenteral Administration of Trypsin. Clinical Effect in 538 Patients**
I. INNERFIELD, A. ANGRIST, and A. SCHWARZ. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **152**, 597–605, June 13, 1953. 1 fig., 12 refs.

Clinical observations on the results of 6,456 infusions of trypsin in 538 patients are reported from the New York Medical College and the Jewish Memorial Hospital, New York, the object being to determine whether this treatment suppressed acute inflammation, whatever the origin.

The technique was as follows: 10 mg. of trypsin was dissolved in 3 ml. of 0·9% sodium chloride solution which, together with 1 ml. of methapyrilene hydrochloride, was added to 100 ml. of 0·9% sodium chloride. Since trypsin in solution rapidly loses its proteolytic action intravenous infusion was started immediately. A typical course of treatment consisted of two infusions, each of 10 mg. of trypsin, daily for 5 to 7 days. To avoid side-reactions the rate of flow did not exceed 30 drops a minute.

The patients were divided into two groups: (1) 110 patients suffering from arteriosclerotic heart disease, hypertensive vascular disease, hypertrophy of the prostate, or diabetes mellitus; and (2) 428 patients suffering from acute inflammation, with thrombophlebitis, rheumatoid arthritis, ulcer of the leg, diabetic gangrene, thrombosis of the central retinal vein, thromboangiitis obliterans, or coronary occlusion.

When the drug was given slowly flushing of the face occurred in 12% of the patients, but there were no other side-effects. In 403 of the 428 patients in Group 2 there was a dramatic subsidence of all signs and symptoms of acute inflammation as the result of treatment, but there was no appreciable change in the controls.

Geoffrey McComas

371. **Observations on the Hemodynamic Properties of a Thiophanium Derivative, Ro 2-2222 (Arfonad), in Human Subjects**
N. S. ASSALI, R. A. DOUGLASS, and R. SUYEMOTO. *Circulation* [*Circulation (N.Y.)*] **8**, 62–69, July, 1953. 6 figs., 12 refs.

The haemodynamic effect of "Ro2-2222" ("arfonad"), a derivative of thiophanium, was studied at the Cincinnati General Hospital (Cincinnati University) in (*a*) healthy subjects, (*b*) healthy subjects over 6 months pregnant, (*c*) patients with acute toxaemia of pregnancy, and (*d*) pregnant patients with essential hypertension. The drug was given intravenously in a dosage varying from 0·03 to 0·2 mg. per kg. body weight, the effect being compared with that of 400 mg. of tetraethylammonium chloride (TEAC). It was found that in doses of less than 0·1 mg. Ro2-2222 had no effect; higher doses in healthy and hypertensive pregnant women resulted in approximately the same fall in blood pressure as that obtained with TEAC, the fall being less marked in the toxaemic patients and non-pregnant subjects. The fall lasted for 3 to 30 minutes, and was accompanied by a rise in skin temperature and decrease in or abolition of the pressor response to cooling of the hand. The effect was at once abolished by injection of 25 mg. of ephedrine.

The authors conclude that the drug acts, like TEAC, as a ganglionic blocking agent. *V. J. Woolley*

372. **Evaluation of a New Antitussive Agent**
L. J. CASS and W. S. FREDERIK. *New England Journal of Medicine* [*New Engl. J. Med.*] **249**, 132–136, July 23, 1953. 2 figs., 14 refs.

The action of *dextro*-3-methoxy-N-methylmorphinan hydrobromide (" dextromethorphan " hydrobromide) as an antitussive agent was compared with those of codeine sulphate and a placebo in 65 patients with severe chronic cough during a 45-day test carried out at Long Island Hospital, Boston, and the Tuberculosis Sanatorium, Cambridge, Massachusetts. The cough-suppressive activity of 4 mg. of dextromethorphan hydrobromide had about 44% of the effectiveness of 17 mg. of codeine, suggesting that, for a comparable effect, 9 or 10 mg. of dextromethorphan would be required. The incidence of side-effects (constipation, drowsiness, or nausea) of 4 mg. dextromethorphan and of placebo tablets was roughly of the same order of magnitude, and was about 15% of that of 17 mg. codeine. The authors suggest that dextromethorphan hydrobromide is an effective antitussive agent, is comparatively free of side-effects, and possibly also devoid of addiction liability, although this property was not specifically investigated.

I. Ansell

373. **Oral Therapy with Mercumatilin (Cumertilin), a New Mercurial Diuretic**
B. E. POLLOCK and F. W. PRUITT. *American Journal o the Medical Sciences* [*Amer. J. med. Sci.*] **226**, 172–176, Aug., 1953. 7 refs.

374. **The Influence of Beer on the Renal Excretion of Water, Sodium and Potassium.** [In English]
J. EK and B. JOSEPHSON. *Acta physiologica Scandinavica* [*Acta physiol. scand.*] **28**, 355–363, July 21, 1953. 5 figs., 8 refs.

The effect of the drinking of moderate amounts of beer on the renal excretion of water, sodium and potassium was studied on a number of healthy human subjects. Beer was found to increase the output of water and sodium and to decrease the potassium excretion. This effect seems to arise in the beer during its fermentation. Beer without hops was effective but not unfermentated malt extract. The alcohol in the beer did not seem to

be responsible for the effect, because a mixture of brandy and water or brandy and malt extract with the same alcohol concentration as the beer was without effect.—[Authors' summary.]

375. **The Effect of Colchicine on the Pituitary Gland and on the Adrenal Cortex.** (Influenza della colchicina sull'ipofisi e sul corticosurrene)
T. Lucherini, C. Summa, and M. Volpicelli. *Policlinico, sezione medica* [*Policlinico, Sez. med.*] **60**, 213–268, July–Aug., 1953. 56 figs., bibliography.

The results are reported of a series of clinical and laboratory investigations which have been carried out at the Rheumatology Centre of the University of Rome into the antirheumatic activity of colchicine and the effect of the drug on pituitary and adrenocortical function. The chief findings were as follows. Colchicine did not appear to increase the therapeutic action of cortisone in rheumatoid arthritis; the improvement noted in 10 patients who received 50 mg. of cortisone intramuscularly and 1 to 2 mg. of colchicine by mouth daily for 20 days showed no appreciable difference from that observed in 10 comparable cases treated with cortisone only in the same dosage. On the other hand, a single dose of 2 mg. of colchicine given by mouth to rheumatic subjects diminished the number of circulating eosinophils by an average of 13·2%, while the same dose given daily increased the urinary excretion of 11-oxysteroids by an average of 39%, suggesting that the drug has some adrenocorticotrophic effect.

In some experiments in animals it was found that colchicine reduced the spreading effect and suppressed some of the histological effects of hyaluronidase injected intradermally. After repeated administration of colchicine to guinea-pigs for 3 to 7 days, histological examination showed evidence of overactivity in the zona fasciculata and zona glomerulosa of the adrenal cortex, an increase in the eosinophil cells of the pituitary gland, and involution of lymphoid tissue, while after 10 days the liver showed vacuolization and glycogen infiltration, the appearances being similar to those found after the administration of cortisone. There were no changes in the pancreas, however, in contrast to the findings after cortisone administration. Colchicine was also shown to cause degenerative changes in the muscle fibres of the heart.

It is concluded that, despite its lack of short-term antirheumatic effect, colchicine has a definite ACTH-like action. Its clinical use over a long period is precluded by its toxic effects. *V. C. Medvei*

376. **How Does Sodium Salicylate Act?** (Comment agit le salicylate de sodium?)
F. Coste, M. Bourel, F. Delbarre, and R. Weissenbach. *Presse médicale* [*Presse méd.*] **61**, 979–982, July 8, 1953. 4 figs., 32 refs.

Historical considerations show that sodium salicylate has always in the past been held to act in accordance with the currently accepted theory of the aetiology of rheumatism. Thus it is not surprising that the discovery of the effect of cortisone in rheumatoid arthritis was soon followed by reports of the development of Cushing's syndrome, of reduction in the peripheral eosinophil leucocyte count, and of changes in urinary 17-ketosteroid excretion in patients receiving large doses of salicylates, while work on experimental animals confirmed that salicylates had certain cortisone-like properties.

However, it is probable that these effects of salicylates result from a purely non-specific stimulation of the pituitary–adrenal axis, since many other substances (collectively described by Selye as " non-specific stressor agents " and including ephedrine, colchicine, atropine, urethane, nitrogen mustards and others) have a similar action, although most of them are completely ineffective in the treatment of the rheumatic diseases. Sodium salicylate must therefore have a specific antirheumatic action in addition to any such non-specific effect on the endocrine glands.

This thesis is supported by the results of experiments carried out by the authors at the Rheumatological Clinic of the Faculty of Medicine of Paris. It was confirmed that sodium salicylate has a direct corticotrophic action, but this was shown to be far too feeble to be responsible for its therapeutic efficacy, the depletion of adrenal ascorbic acid caused by clinically effective doses of salicylate being far less than that resulting from therapeutically effective doses of ACTH. Again, whereas quite small doses of ACTH or cortisone definitely increased urinary corticosteroid excretion in 5 healthy subjects, large doses of sodium salicylate had no demonstrable effect. It must thus be concluded that, although sodium salicylate has an undoubted stimulant action on the pituitary–adrenal axis, the mechanism by which it exerts its specific therapeutic effect remains unknown.
Adrian V. Adams

377. **A New Series of Highly Active Local Anesthetics**
F. P. Luduena, R. O. Clinton, and S. C. Laskowski. *Science* [*Science*] **118**, 138–139, July 31, 1953. 7 refs.

The most marked local analgesic action in a series of 2-alkoxythiolbenzoates, substances allied to procaine, tested at the Sterling-Winthrop Research Institute, Rensselaer, New York, was obtained with " WIN 4510 " (the β-diethylaminoethyl ester of 2-*n*-hexyloxy-4-aminothiolbenzoic acid hydrochloride). This compound was 117 times as active as procaine when injected intracutaneously in the guinea-pig, and 330 times as active when given intraspinally in the rabbit. When applied to the cornea or injected into the urethra of the rabbit the activity was 500 and 1,000 times respectively that of cocaine. The *n*-propoxy (" WIN 3766 ") and *n*-butoxy (" WIN 3800 ") compounds were also much more active than procaine and cocaine.

WIN 4510, however, was 160 times as toxic as procaine and 60 times as toxic as cocaine when injected intravenously in the mouse. Toxicity increased with the length of the alkoxy side-chain; the most favourable ratio of activity to toxicity was shown by WIN 3766. In laboratory tests, all three compounds were more active by topical application, and had a greater margin of safety, than " tetracaine " (amethocaine) or " dibucaine " (cinchocaine). *L. G. Goodwin*

Chemotherapy

378. **Effects of Cancer Chemotherapeutic Agents on Dehydrogenase Activity of Human Cancer Tissue *in vitro***
M. M. Black and F. D. Speer. *American Journal of Clinical Pathology* [*Amer. J. clin. Path.*] **23**, 218–227, March, 1953. 4 figs., 6 refs.

The dehydrogenase activity of specimens of tissue from various forms of human carcinoma, obtained at operation at the Flower and Fifth Avenue Hospitals, New York, was determined by the "tetrazoleum technique" (measurement of the rate of reduction of the colourless salt 2 : 3 : 5-triphenyltetrazolium chloride to its red formazan derivative). The effect *in vitro* of urethane and triethylene melamine, alone and combined, on the dehydrogenase activity of these tissues was also studied.

The results revealed considerable variation in effect between different specimens of the same type of tumour, but no apparent correlation was observed between dehydrogenase activity of the tissue specimen and the clinical behaviour of the tumour.

There was some indication that the effect *in vitro* of urethane on the dehydrogenase activity ran parallel with the *x*-ray sensitivity of the tumour. A combination of the two chemotherapeutic agents sometimes enhanced the inhibition effect *in vitro*. *L. A. Elson*

379. **Laboratory Techniques for the Determination of Sensitivity of Tubercle Bacilli to Isoniazid, Streptomycin, and P.A.S. (M.R.C. Isoniazid Trial: Report No. 3)**
Tuberculosis Chemotherapy Trials Committee of the Medical Research Council. *Lancet* [*Lancet*] **2**, 213–217, Aug. 1, 1953. 2 figs., 20 refs.

380. **Antibiotics and Their Action on Pathogenic Fungi. I. Penicillin and Streptomycin**
F. Raubitschek. *Journal of Investigative Dermatology* [*J. invest. Derm.*] **20**, 401–403, June, 1953. 4 refs.

The addition of streptomycin or penicillin to media for routine culture of dermatophytes is widely used in medical mycology. The antibiotics reduce bacterial contamination in primary isolations and allow the slow-growing fungi to develop, thus increasing the number of positive fungal cultures, but they do not inhibit, and indeed may enhance, growth in the saprophytic life-phase on artificial media. Low yields on primary isolation seem to be due to the inability of fungi to change from a parasitic to a saprophytic life-phase, the two phases being morphologically and possibly also physiologically different.

The author, working at the Hebrew University–Hadassah Medical School, Jerusalem, has studied the effect of penicillin and streptomycin on these two life-phases. In the first of two experiments slants of Sabouraud's maltose–agar medium with and without 5 units of penicillin or 50 units of streptomycin per ml. were prepared. The material planted out included skin scales, hairs, and nail clippings from various mycotic and non-mycotic affections; they were incubated for at least 3 weeks at 26° C. In the second experiment Petri dishes containing 20 ml. of Sabouraud's agar with 0, 2·5, 5, 10, 20, 50, 100, and 500 units of penicillin per ml., 0, 5, 10, 20, 25, 50, 100, and 500 units of streptomycin per ml. and 5 units of penicillin plus 50 units of streptomycin per ml. were prepared. These were inoculated with stock strains of *Trichophyton mentagrophytes*, *T. rubrum*, *T. violaceum*, and *T. schoenleini* in duplicate, and incubated upside down at 26° C. for 4 weeks, the colony size being noted every 3 days. The results of the first experiment showed that of 409 samples grown, 305 were positive for fungi microscopically, and 169 of these gave positive cultures on plates containing antibiotics compared with 90 on plates without. Again, 64% of the colonies were visible at 3 to 5 days in the former compared with 60% at 7 to 10 days in plates without antibiotics. Macroscopical identification was possible in media containing antibiotics in half the time required for those without antibiotics. In the second experiment each of the organisms grew equally well on the plates with or without antibiotics, these having apparently no effect on colony size or morphology. No enhancement of growth was observed, however, with the laboratory strains of dermatophytes. From this preliminary study the author concludes that these antibiotics appear to activate the adaptation of fungi from a parasitic to a saprophytic life.
Malcolm Woodbine

381. **Inhibition of Respiration by Aureomycin and Terramycin**
D. T. O. Wong, S. Barban, and S. J. Ajl. *Antibiotics and Chemotherapy* [*Antibiot. and Chemother.*] **3**, 607–612, June, 1953. 2 figs., 8 refs.

Aureomycin and oxytetracycline ("terramycin") were found to inhibit oxygen consumption by a sensitive strain of *Bacterium coli in vitro* in the presence of various substrates which participate in microbial oxidation processes. It appears likely that these antibiotics produce this effect by disturbing the phosphorylating mechanisms involved in the process of oxidation.
A. W. H. Foxell

382. **Clinical Problems Pertaining to Neurotoxicity of Streptomycin Group of Drugs**
J. Winston. *Archives of Otolaryngology* [*Arch. Otolaryng.* (*Chicago*)] **58**, 55–61, July, 1953. 31 refs.

It is now well known that damage to vestibular and cochlear mechanisms may complicate use of the streptomycin group of drugs. Dihydrostreptomycin, the hydrogenated form of the antibiotic, has no therapeutic advantage over streptomycin; it was developed in the hope that it would not produce the 8th-nerve complications which are frequent with the parent drug, but this hope

has been disappointed. While streptomycin frequently damages the vestibular apparatus, it seldom damages the cochlear, whereas dihydrostreptomycin frequently causes deafness as well as severe damage to the vestibular mechanism. The deafness due to streptomycin, which is usually preceded by tinnitus, in the author's experience " practically never " occurs with doses of less than 3 g. per day and moreover is found in only 1% of patients even under heavy dosage; also, if the damage is moderate, the hearing may be recovered. There is still doubt as to whether the damage is peripheral or central, or both. The author regards it as primarily central, although the end-organ may be attacked. This view is supported by the results of galvanic stimulation, which is now believed to affect the ganglia and tracts rather than the end-organ.

In discussing whether pregnancy is a contraindication to the use of streptomycin, the author recalls that although it has been shown that streptomycin crosses the placenta, experiments in animals have not shown any neurotoxic effects on the foetus, and such little clinical evidence as is available for human subjects supports this view. It has also been suggested that streptomycin might be used to destroy the vestibular labyrinths in cases of intractable Ménière's disease. The author is opposed to this practice, pointing out that streptomycin greatly diminishes, but does not entirely abolish, the recurrent vertigo, and as it attacks the central vestibular mechanism it may attack other brain structures as well. In conclusion, he suggests that valuable information would be obtained, and much trouble avoided, if audiometric and vestibular examinations were carried out before streptomycin treatment is started rather than after the first signs of neurotoxicity have appeared.

F. W. Watkyn-Thomas

383. **The Action of Carbomycin (Magnamycin) on Some Viral and Rickettsial Infections**

S. C. WONG, C. G. JAMES, and A. FINLAY. *Antibiotics and Chemotherapy* [*Antibiot. and Chemother.*] **3**, 741–750, July, 1953. 10 refs.

Carbomycin (" magnamycin "), a new antibiotic derived from *Streptomyces halstedii*, is characterized by its low toxicity and the high solubility of its salts in water, higher concentrations of the drug being reached in various body tissues than in the blood. Its bacterial spectrum is similar to that of penicillin. It has been shown that little or no cross-resistance exists between carbomycin and seven other commonly used antibiotics. In the studies of its activity in rickettsial infections here described from the Pfizer Research Laboratories, Brooklyn, New York, embryonated hens' eggs were employed in the first part of the study.

Antibiotic activity was demonstrated against the following rickettsiae and viruses: *Rickettsia prowazekii*, *R. typhi*, *R. akari*, *R. tsutsugamushi*, *R. rickettsii*, *R. conorii*, the causal organism of North Queensland tick typhus, *Coxiella burnetti*, and the viruses causing psittacosis, ornithosis, lymphogranuloma venereum, human and feline pneumonitis, and sporadic bovine encephalomyelitis. In studies carried out *in vivo* carbomycin showed effective therapeutic activity in mice infected with psittacosis, rickettsial pox, and scrub typhus, and against epidemic typhus in the guinea-pig. Its effect compared favourably with that of aureomycin in experimental infection with *R. tsutsugamushi*. It was not effective in mice infected with herpes simplex, meningo-encephalomyelitis, rabies, vaccinia, or poliomyelitis Type-II virus. It was also ineffective, as measured by the survival ratio, in animals infected with the virus of psittacosis or of lymphogranuloma venereum intracerebrally, probably, the authors suggest, because the antibiotic cannot pass the blood–brain barrier in sufficient quantity, or because it is inactivated *in situ* by the brain tissues.

A. W. H. Foxell

384. **The Absorption and Excretion of " Spirotrypan ", a New Antisyphilitic Drug of the Arsenobenzol Group.** (Über Resorption und Ausscheidung von Spirotrypan, einem neuen Antiluicum der Arsenobenzolreihe)

W. HERRMANN and L. THER. *Archiv für Dermatologie und Syphilis* [*Arch. Derm. Syph. (Berl.)*] **195**, 670–685, 1953. 8 figs., 23 refs.

The absorption of " spirotrypan ", a new antisyphilitic drug of the arsphenamine group, can be determined quantitatively by estimation of its arsenic component. The assays on organs, urine, and faeces here described were performed by wet ashing by the method of Hubbard, and the arsenic content estimated by the method of Gutzeit and Lockemann.

Experiments in the rat showed that the absorption of spirotrypan following intramuscular injection rose to more than 80% during the first 24 hours, but about 5% of the conjugated material was still to be found at the site of injection 10 days later. Local compatibility was good. Multiple injections, also made intramuscularly, in the dog produced no noticeable histo-pathological changes. The blood level of the drug in the rat reached its maximum 3 hours after an intramuscular injection and fell in a fluctuating manner for up to 10 hours, after which a fairly constant level was established; 7 days later the level was still definitely above the level in control animals. Studies of the persistence of spirotrypan in the organs of rabbits made 17 days after the last of 4 injections showed that the greatest amounts were stored in the skeletal muscles, skin, and liver; in the guinea-pig the highest arsenic concentrations were found in the kidneys, skeletal muscle, spleen, and liver. In the guinea-pig's liver the arsenic was stored predominately in the Kupffer cells, while in the rabbit it was found mostly in the liver parenchymal cells.

Excretion of the drug in the rabbit was similar in amount and rate after both intravenous and intramuscular injection. In 10 days half of the administered arsenic had been eliminated, two-thirds of it through the kidneys and one-third by way of the intestine, in the latter case largely in the bile. Following intravenous injection the concentration of arsenic in the urine on the first day was higher than after intramuscular administration.

Norval Taylor

See also Gastroenterology, Abstract 457; and Cardiovascular System, Abstract 491.

Infectious Diseases

385. **Histoplasmosis in Great Britain. Description of a Second Case of Disseminated Histoplasmosis; Treatment by Ethyl Vanillate**
S. LOCKET, E. A. ATKINSON, and W. S. M. GRIEVE. *British Medical Journal* [*Brit. med. J.*] **2**, 857–860, Oct. 17, 1953. 5 figs., 12 refs.

After a brief review of the cases of *Histoplasma* infection previously published in Great Britain the second case of disseminated histoplasmosis to be reported is described. This case was fatal in spite of treatment with 45 to 50 g. of ethyl vanillate daily. Some information is included on culture of the organism, as in this case it showed certain cultural peculiarities.—[Authors' summary.]

386. **Sarcoidosis—a Clinical, Prognostic Follow-up Study.** [In English]
S. E. FAGERBERG. *Acta medica Scandinavica* [*Acta med. scand.*] **146**, 239–251, Aug. 19, 1953. 24 refs.

The results are reported of a follow-up study of 54 cases of sarcoidosis (25 in males, 29 in females) diagnosed at the Falu Hospital, Falun, Sweden, during the years 1944–51. Of these 54 patients, 6 had died (post-mortem reports on 2 of these being included), while 5 were incapacitated by severe changes in the lungs and eyes. Only 10 patients were symptomless with no clinical evidence of the disease after a mean observation period of 5·4 years; 9 others, though symptomless, had signs of the disease in the lungs, eyes, or skeletal system, and the remaining patients showed both signs and symptoms of the disease, but were not severely incapacitated.

The author concludes that the prognosis in sarcoidosis cannot be regarded as good, since it often causes considerable incapacitation and the mortality is not insignificant. *D. G. Adamson*

387. **Vegetative Neuritis, Possibly Epidemic.** (Neuritis vegetativa (epidemica?))
T. FOG. *Ugeskrift for Læger* [*Ugeskr. Læg.*] **115**, 1244–1251, Aug. 13, 1953. 2 figs., 6 refs.

The author describes 10 cases of what is considered to be a new, infectious, and probably epidemic disease. Half the patients were admitted to the Kommunehospitalet, Copenhagen, the others being treated at home. All 10 patients were women aged between 20 and 40, but in view of the small number of cases this sex distribution is thought not to be representative. The cases occurred during the Copenhagen poliomyelitis epidemic of 1952–3, and 3 of the patients had been in close contact with cases of this disease immediately before the start of their attack.

The illness was characterized by the sudden onset, in previously healthy individuals, of occipital headache which was sometimes associated with dizziness, nausea, and vomiting, and a mild pyrexia of at most 38° C. (100·4° F.). During the active phase, which lasted for 1 to 3 weeks, the patients complained of paraesthesiae, which were usually confined to one or more of the extremities, appearing especially in the fingers. This was often associated with circulatory disturbances of the hands or feet, manifested by extreme coldness, cyanosis, and in some cases a profuse cold sweat. Other symptoms at this time included some neck stiffness, pain in the back and thighs, diarrhoea, and profound prostration. After about 3 weeks some improvement usually occurred and lasted a few weeks, but this was followed by a relapse with a return of the paraesthesiae, muscular weakness and tenderness, slight pyrexia, and vascular disturbances. Further relapses were not uncommon, and some patients were not completely well until many months after the first onset. Paralysis occurred in one case, but there was no evidence of anterior horn cells being affected.

Physical examination during the active phase revealed little beyond weakness of one or other limb, occasionally a diminished tendon jerk, scattered hypoaesthaesia, and circulatory disturbances of the extremities. Lumbar puncture, which was carried out on 5 patients in different phases of the disease, yielded in every case a normal spinal fluid. Electromyography, performed in 2 cases, showed weakness of root or peripheral origin. Electroencephalograms, also obtained in 2 cases, were normal. The nosological problem is discussed.

H. F. Reichenfeld

VIRUS DISEASES

388. **Post-inoculation Poliomyelitis**
J. GRANT. *British Medical Journal* [*Brit. med. J.*] **2**, 66–70, July 11, 1953. 9 refs.

The author reviews previous reports in the literature of poliomyelitis occurring after the intramuscular injection of diphtheria or pertussis antigens, and gives details of an epidemic of poliomyelitis which began on South Tyneside (Gateshead and neighbourhood, for which the author is Medical Officer of Health) in the spring of 1952 and comprised 138 cases, of which 118 were treated in hospital. Of these, 8 arose at varying intervals (in most cases 10 to 18 days) after the intramuscular injection of prophylactic, for diphtheria in 4 cases, and for diphtheria and pertussis combined in the other 4, and 7 of the 8 patients, all under 9 years of age, developed paralysis. There were no definite cases occurring after the intramuscular injection of other substances such as penicillin or streptomycin. As soon as these cases were noticed intramuscular inoculations were stopped in the Gateshead clinics, and general practitioners were advised to restrict immunization to the subcutaneous use of A.P.T. or P.T.A.P.

It was calculated that in the age group 6 months to 2 years the attack rate of poliomyelitis in the period

May to August, 1952, was 1 in 87 for recently inoculated children against 1 in 211 for the control group, that is, those not recently inoculated. Paralysis in the former group (7 cases) occurred in the inoculated arm in 3 cases and in the inoculated leg in one; in one the inoculated arm and the opposite arm and leg were involved, while in 2 others the ocular muscles and the opposite leg respectively were affected. In discussing the pathology of the condition the author suggests that trauma to the muscles caused by the inoculation enables the virus already present in the patient to attack the motor cells in the spinal cord which supply the damaged muscles. He concludes that there is no doubt of the increased risk of an attack of poliomyelitis developing as a result of intramuscular immunizing injections given when the disease is prevalent, and suggests that immediately the first case of post-inoculation poliomyelitis is confirmed, such injections should cease for a time, as recommended by the Ministry of Health. It is probable that if manufacturers could produce antigens which would be satisfactory when given by subcutaneous injection, the risk would be greatly reduced. Finally, the medico-legal aspect of the problem is briefly mentioned.

J. V. Armstrong

389. **Follow-up Study in Seventy-five Cases of Non-paralytic Poliomyelitis**

E. Moskowitz and L. I. Kaplan. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **152**, 1505–1506, Aug. 15, 1953. 1 ref.

The authors re-examined 75 patients who had had non-paralytic poliomyelitis 1½ to 6 years before. Muscle weakness was noted in 29 cases (38·6%), but in only 7 of these were there symptoms referable to the site of muscular weakness. The muscles affected were mainly those concerned with weight-bearing, especially those of the calf and quadriceps group. The occurrence or site of muscular weakness was in no way related to a loss or diminution of tendon reflexes during the acute phase of the illness, to the duration of stay in hospital, or to the duration of bed rest.

Of the 75 patients examined, 42·7% stated that they readily became fatigued and 24% showed evidence of emotional disturbances, such as irritability, instability, and stuttering. [The authors do not define the terms " irritability " and " instability ", and do not state how the incidence in their patients compared with that in the normal population.] *R. S. Illingworth*

390. **Poliomyelitis in Children under 6 Months in England and Wales during 1950**

D. H. Geffen and S. Tracey. *British Medical Journal* [*Brit. med. J.*] **2**, 427–429, Aug. 22, 1953. 5 refs.

The authors analyse 82 cases of poliomyelitis in children under the age of 6 months which were notified in England and Wales during 1950. The paralytic form of the disease was found in 77 cases and the non-paralytic in 5.

The total number of notifications of paralytic poliomyelitis in children under 15 years was 3,799, and the number of children under 6 months of age per 1,000 under 15 was 35·8. The actual incidence of paralytic poliomyelitis in children under 6 months was 56·6% of that which would be expected had the disease been distributed evenly in 6-month age groups up to 15 years. It is suggested that the low incidence of non-paralytic poliomyelitis was due to difficulty in diagnosis.

Of the 82 patients, 19 died (23%); the corresponding figures for all ages above 6 months were 715 deaths out of 7,668 (9·3%). Of 24 children under 9 weeks of age, 9 died, a mortality rate of 37·5%. There was severe residual paralysis in 2 or more limbs of 30 of the surviving 58 patients. In 6 instances mother and baby contracted the disease at the same time, or within a few days or weeks of each other.

The authors were unable to reach any conclusions concerning the influence of breast-feeding; they also were unable to find symptoms which were characteristic of the pre-paralytic stage. They emphasize the danger of poliomyelitis in young infants, and suggest that prophylactic inoculations—for example, against diphtheria and whooping-cough—during an outbreak of poliomyelitis should be postponed in children under the age of 6 months. *L. J. M. Laurent*

391. **Cardiac Manifestations of Poliomyelitis**

M. J. Fox, L. Sennett, and J. F. Kuzma. *Lancet* [*Lancet*] **2**, 323–324, Aug. 15, 1953. 3 figs., 8 refs.

Electrocardiographic examination of 189 patients with acute anterior poliomyelitis in hospitals in Milwaukee, Wisconsin, revealed abnormalities in 61 cases. The records showed transient T-wave changes in 24 cases, transient ST–T changes in 24 cases, and tachycardia of more than 140 beats per minute in 5 cases, intraventricular block, S–T depression, and arrhythmias being among the abnormalities encountered in the remaining cases. Abnormalities were found in the electrocardiograms of 3 out of 9 patients suffering from bulbar poliomyelitis. Usually the changes were detected during the first week of the illness, and sometimes even on the first day. In no instance was the abnormality considered to be characteristic of poliomyelitis. Only 4 patients showed clinical evidence of myocarditis.

The heart was examined at necropsy in 70 cases of bulbar poliomyelitis, 25 of which were in patients over 10 years of age. Apart from petechial haemorrhages no pathological changes were found macroscopically. On histological examination, however, interstitial inflammatory reactions were detected in 38 cases, equally distributed between the two sexes. The changes were mild to moderate in degree, and never so severe as those found in cases of Fiedler's isolated myocarditis. The myocardial fibres showed fragmentation and separation, and varied in intensity of staining. Oedema and inflammatory cells were observed in the interstitial areas. The chief inflammatory cells were polymorphonuclear leucocytes, but lymphocytes and histiocytes were also found. For the most part the changes were encountered in the subendocardium and in association with minor interstitial haemorrhages.

Despite these electrocardiographic, clinical, and histological findings, there is insufficient evidence to show

whether myocarditis is a specific complication of poliomyelitis. It does not appear to be associated with anoxia or with bulbar involvement. Further investigation to determine whether the three strains of poliomyelitis virus are cardiotropic in varying degrees may explain the wide differences in incidence of myocarditis as reported by different authors. *A. Garland*

392. **The 1952 Outbreak of Encephalitis in California. Differential Diagnosis**
R. H. KOKERNOT, H. R. SHINEFIELD, and W. A. LONGSHORE. *California Medicine* [*Calif. Med.*] **79**, 73–77, Aug., 1953. 1 fig., 23 refs.

During 1952 in the Central Valley of California there was an epidemic of arthropod-borne St. Louis and Western equine encephalitis. In this paper the clinical features in 386 laboratory-confirmed cases (38 due to infection with the St. Louis virus and 348 to Western equine virus) are discussed under the different age groups, since it was observed that symptoms varied with the age of the patient.

In 94 infants under 1 year of age the disease, which was due to the Western equine virus, was characterized by sudden onset of fever accompanied by convulsions; the temperature was usually above 102° F. (38·9 C.) and remained high despite chemotherapy. In patients between 1 and 14 years (105) there was a more insidious onset, with fever, headache, vomiting, drowsiness, irritability, and restlessness, accompanied by nuchal rigidity and tremor. In 187 patients of 15 years and over the onset was " grippe-like ", with malaise, lethargy, drowsiness, fever, and headache so severe as to dominate all subjective symptoms. This was soon followed by signs of meningeal irritation. In this group 24 patients became comatose and were incontinent for 3 or 4 days; the authors suggest that this is probably the " only brain condition in which unconsciousness may persist without being followed by death or gross disability ". Paralysis of the legs occurred in one patient, and bulbar signs necessitating tracheotomy in 2 patients. It is pointed out that these last symptoms, which are suggestive of poliomyelitis, indicate the difficulty of differential diagnosis, which cannot usually be reached by clinical observation. A precise aetiological diagnosis can be made only by isolation of the virus or by suitable serological tests. Examination of the cerebrospinal fluid was comparatively unhelpful, since there was a wide variation in the number and type of cells. An initial preponderance of polymorphonuclear leucocytes was followed by a lymphocytosis in the spinal fluid.
D. Geraint James

393. **The 1952 Outbreak of Encephalitis in California. Laboratory Methods for Etiologic Diagnosis**
E. H. LENNETTE, M. C. NYBERG, D. M. BARGHAUSEN, R. CHIN, F. Y. FUJIMOTO, and M. K. ITATANI. *California Medicine* [*Calif. Med.*] **79**, 78–83, Aug., 1953. 7 refs.

In this second paper in the series on the oubreak of encephalitis in California in 1952 [see Abstract 392] methods used in diagnosis are discussed.

Isolation of the virus from the cerebrospinal fluid, the blood, or nervous tissue can be attempted, but in the authors' experience neither the cerebrospinal fluid nor the blood proved a practical source, the former, it is suggested, because the specimen had been too long in transit under unfavourable conditions before reaching the laboratory, and the latter because the stage of viraemia occurred early, often before the patient had sought medical advice. Material from more than 1,500 patients was examined during the summer months, and infection with Western equine virus was established in 370 and with St. Louis virus in 44. In only 5 of the 370 cases of Western equine encephalitis was the diagnosis made by isolation of the virus in specimens of tissue from the central nervous system, but in addition, the infection in some cases [number unspecified] was said to be due to the viruses of mumps and herpes simplex. The diagnosis of Western equine encephalitis was confirmed in 356 cases by a complement-fixation test *in vitro* and in 9 by determination of the serum-neutralizing antibodies in mice.

The complement-fixation test was considered positive if there was a 4-fold or greater increase in titre in convalescent serum compared with serum taken during the acute phase, the blood being withdrawn at intervals of 10 days or longer. The neutralization test did not provide such a clear-cut difference between a specimen taken during the acute stage and one taken during the convalescent stage, since in the former there was already a high titre of neutralizing antibodies. *D. Geraint James*

394. **The 1952 Outbreak of Encephalitis in California. Epidemiologic Aspects**
A. C. HOLLISTER, W. A. LONGSHORE, B. H. DEAN, and I. M. STEVENS. *California Medicine* [*Calif. Med.*] **79**, 84–90, Aug., 1953. 6 figs., 5 refs.

The epidemiological aspects of the outbreak of encephalitis in California in 1952 [see Abstracts 392 and 393] are described in this third paper. Although the outbreak, so far as cases in human beings were concerned, was confined to the Central Valley of California, there was, during the same period, an epidemic of encephalitis in horses throughout the State. It is believed that a horse which is clinically ill with Western equine encephalomyelitis is no longer a hazard to neighbouring horses and human beings, since in the stage of overt illness viraemia is no longer present. Viraemia lasts about 5 days, during which time it is theoretically possible for mosquitoes to bite the animal and transmit infection to other animals and to man. According to present knowledge, St. Louis encephalitis does not cause clinical illness in the horse, although a serological survey revealed evidence of antibodies to the St. Louis virus in one-third of adult horses. Although large numbers of horses are vaccinated annually, the incidence of the disease is higher in horses than in man, probably because of the former's greater susceptibility to the disease or greater exposure, both as to the number of vectors and the area of unprotected skin.

As regards the age and sex distribution of the disease in man, no case of St. Louis encephalitis was found

among infants under one year, but one-third of all the cases of Western equine encephalitis occurred in that age group. The ratio of males to females with Western equine encephalitis was 2 to 1; with St. Louis encephalitis it was only 1·2 to 1. This sex disparity has been attributed by some workers to greater occupational exposure [but this could hardly be the explanation for such a difference in the age group 5 to 9 years].

D. Geraint James

395. **The 1952 Outbreak of Encephalitis in California. Vector Control Aspects**

F. M. STEAD and R. F. PETERS. *California Medicine* [*Calif. Med.*] **79**, 91–93, Aug., 1953.

In the fourth paper in this series measures for the control of vectors of encephalitis are discussed. The disease is known to be transmitted by a mosquito, *Culex tarsalis* being the usual vector in California. It is believed that the epidemic in 1952, despite the large-scale control measures which were already in operation, was due to more extensive cultivation of land following improved methods of irrigation and favourable climatic conditions—both factors contributing to an increased area of ideal breeding places for the mosquito—and to the emergence of D.D.T.-resistant vectors. The measures which were accordingly introduced as a matter of urgency included the "fogging" of towns with an insecticide aerosol, the establishment of a barrier around each town by spraying, and the intensive treatment of all mosquito-breeding areas near towns.

The authors state that in the future, more intensive ecological studies of *Culex tarsalis* are to be undertaken, information is to be obtained of the number of adult mosquitoes in every part of the Central Valley, and during the summer months mosquitoes are to be examined for virus content.

D. Geraint James

396. **The 1952 Outbreak of Encephalitis in California. Long Term Neurologic and Psychiatric Studies of Sequelae**

K. H. FINLEY and W. M. CHAPMAN. *California Medicine* [*Calif. Med.*] **79**, 94–96, Aug., 1953. 12 refs.

The authors of the fifth paper in this series state that the neurological and psychological sequelae, if any, among the patients who contracted encephalitis in California in 1952, are being studied. Apart from a recurrence of convulsions in 2 infants, no abnormality has been observed to date.

D. Geraint James

397. **Bornholm Disease in Children**

M. E. DISNEY, E. M. HOWARD, B. S. B. WOOD, and G. M. FINDLAY. *British Medical Journal* [*Brit. med. J.*] **1**, 1351–1354, June 20, 1953. 18 refs.

The clinical features and virological findings in 104 typical cases of Bornholm disease in children admitted to the medical and surgical wards of Dudley Road Hospital, Birmingham, are described. In all these cases there was an acute onset of abdominal or chest pain, injected fauces, and headache or meningism, lasting about 5 days and associated with recrudescence in half the cases. The abdominal signs were such that laparotomy was performed in 9 cases before Bornholm disease was suspected. The chest pain was associated with a pleural rub in 7 cases and crepitations in 10 cases. Faecal suspensions were inoculated intracerebrally and intraperitoneally into new-born mice, and a Group-B, Type-3 Coxsackie virus was isolated from half the cases. The authors also give a brief account of 26 atypical cases; these could be divided into four groups: neurological (7 cases), pyrexia of unknown origin (10), pneumonitis (4), and infantile, in which there were screaming attacks, fever, malaise, and recovery unaffected by treatment (5). A virus was isolated from 3 of 13 specimens of faeces examined.

[The paucity of data concerning the strain of virus isolated and the rise in neutralizing antibodies renders the report on these cases inconclusive, especially in view of the ubiquitous nature of the Coxsackie family of viruses.]

D. Geraint James

398. **The Isolation of a Coxsackie Virus from Two Cases of Bornholm Disease**

R. H. A. SWAIN and R. G. MITCHELL. *British Medical Journal* [*Brit. med. J.*] **1**, 1354–1356, June 20, 1953. 8 refs.

The results are recorded of virus studies carried out on specimens of faeces and blood taken from 2 children suffering from typical Bornholm disease admitted to the Royal Hospital for Sick Children, Edinburgh, during an epidemic in that city in the summer of 1951. Both children were seized suddenly with acute abdominal pain, spasmodic in nature, with complete and uneventful recovery soon after admission to hospital. A 20% ether-treated suspension of faeces injected intracerebrally and intraperitoneally into suckling mice produced infiltration of the meninges and necrosis of muscle and brain tissue. From the faeces of both children, a Group-B Coxsackie virus was isolated. Specimens of serum taken in the acute and convalescent phases of the disease were tested for neutralizing antibodies to the virus isolated. These were present in the serum taken in the convalescent phase 3 weeks after the onset of the illness, and had disappeared from serum 8 months later.

D. Geraint James

399. **Virus and Virus Antigen in the Blood of Smallpox Patients. Their Significance in Early Diagnosis and Prognosis**

A. W. DOWNIE, K. MCCARTHY, A. MACDONALD, F. O. MACCALLUM, and A. D. MACRAE. *Lancet* [*Lancet*] **2**, 164–166, July 25, 1953. 1 fig., 5 refs.

Blood from 28 patients with variola major, 16 of whom recovered and 12 died (4 from acute haemorrhagic smallpox), was examined at the University of Liverpool and the Virus Reference Laboratory, Colindale, London, for virus and antigen. For the detection of virus the chorio-allantoic membranes of 2 to 6 chick embryos were inoculated with the blood, and the number of variola lesions counted after 3 days. Experiments showed that an inoculum of blood cells mixed with serum gave essentially the same results as lysed whole blood or lysed cells and clot without serum. Serum by itself yielded less virus and was used only in one case. Storage of blood

at 4° C. for 1 to 4 weeks was found to cause loss of virus. In many cases cultures were not made until 12 to 48 hours after the blood had been collected from the patient, and the authors consider that the number of positive cultures would have been higher had there been no such delay.

Virus was cultured in 11 out of the 12 fatal cases from blood which was taken between the 1st and 8th days of the illness, and in 3 of the remaining 16—the blood in these 3 being taken on the 1st or 2nd day and the amount of virus being much less than in the fatal cases. When the findings in series previously reported by the same authors are included, a total of 29 specimens from 25 non-fatal cases yielded 4 positive cultures, all from blood taken in the first 2 days and all of low virus content, whereas 23 specimens from 18 fatal cases gave 19 positive cultures, most of them with high virus content. The authors consider the presence of more than a few infective doses in cultures from 0·1 ml. of blood at any stage of the disease, or the presence of virus in the blood at all after the first 2 days, to indicate a very bad prognosis.

In 22 cases the blood was tested for virus antigen by a complement-fixation test, which gave negative results in 12 non-fatal cases, whereas of 10 fatal cases tested, the results were negative in 4 and positive in 6 (including 3 acute haemorrhagic cases, in which the titre was high). There was no correlation in individual cases between the amount of virus present and the antigen titre. The presence of antigen in the blood is also considered to indicate a bad prognosis. *M. Lubran*

400. **Family Outbreaks of Infectious Hepatitis. Prophylactic Use of Gamma Globulin**
B. F. Brooks, D. Y. Hsia, and S. S. Gellis. *New England Journal of Medicine* [*New Engl. J. Med.*] **249**, 58–61, July 9, 1953. 1 fig., 23 refs.

The family contacts of 64 patients with infective hepatitis seen at the Children's Medical Center or the Beth Israel Hospital, Boston, were divided into two groups without selection; gamma globulin was given to the 55 immediate members (22 being under 15 years old) of 17 families and to none of the 114 members (51 under 15) of the remaining 29 families, which served as controls. The usual dose was 0·1 ml. of gamma globulin per lb. (0·22 ml. per kg.) body weight, with a maximum of 5 ml. in infants and children and 10 ml. in adults. Hepatitis developed in 18 members (all children) of 14 of the 29 families not treated with gamma globulin, whereas among the family contacts treated with the material only one adult developed jaundice—2 days after the gamma globulin had been given.

The authors conclude that there is a high incidence of infective hepatitis among children exposed to infection within the family group, that gamma globulin is effective in preventing this spread, and that in adults involved in these outbreaks immunity is high. They consider that the administration of gamma globulin is definitely indicated when sick children are exposed to hepatitis, but point out that in healthy children the disease is relatively more benign than in adults, though not free from danger. Passive immunization may be justified in adult contacts in certain circumstances, especially in cases of pregnancy and chronic illness. The optimum dosage to avoid waste has not yet been determined, and the possibility of using small doses to modify rather than prevent the attack requires further study.

K. C. Robinson

401. **Studies of the Natural History of Herpes Simplex Infections**
G. J. Buddingh, D. I. Schrum, J. C. Lanier, and D. J. Guidry. *Pediatrics* [*Pediatrics*] **11**, 595–610, June, 1953. 11 figs., 17 refs.

The natural history of primary and recurrent infection with the virus of herpes simplex was studied in 12 children with herpetic stomatitis at the Charity Hospital, New Orleans. The virus was isolated from the mouth and stools during the acute stage, during convalescence, and also later, but was not isolated from the blood or cerebrospinal fluid. Neutralizing antibodies were first detected in the serum between the fourth and seventh days of the disease, a maximum level being attained during the second or third week, although there was considerable variation in individual antibody titres.

In addition, herpes simplex virus was isolated from the mouth of a number of healthy subjects, especially children between the ages of 7 months and 2 years. It was recovered from 12% of white and 26% of negro children in this age group. It is pointed out that the percentage of children without neutralizing antibodies in the serum was highest in this age group, as also was the incidence of cases of primary herpetic gingivo-stomatitis. Neutralizing antibodies were found with increasing frequency in subjects over the age of 2 years; at age 15 and over they were found in 90% or more. The serum of 79% of white and 93% of negro infants under the age of 6 months contained neutralizing antibodies. Since it is demonstrable that these antibodies traverse the placental barrier freely, such figures could be accounted for by passive transfer from the pregnant mother.

D. Geraint James

BACTERIAL DISEASES

402. **Treatment of Tularaemia of the Respiratory Tract with Streptomycin.** (Лечение больных туляремией дыхательных путей стрептомицином)
R. A. Savel'eva and G. P. Uglovoi. *Клиническая Медицина* [*Klin. Med. (Mosk.)*] **31**, 47–50, June, 1953. 2 figs.

Tularaemia is a fairly common disease in parts of the U.S.S.R., and frequently attacks the respiratory tract. In this paper the authors describe the effects of streptomycin in the treatment of 10 such cases in patients aged from 19 to 43 years, in 4 of which the disease was of bronchitic, 3 of bronchopneumonic, and 3 of pleuropneumonic type; the severity of the condition tended to increase from the first type to the last. Treatment was begun between the 8th and the 17th day of the disease, and in 2 or 3 days the temperature fell, the general condi-

tion being much improved; chest pains disappeared, as did cough and sweating, and sleep and appetite returned, Resolution of the pulmonary fields, however, took much longer. Treatment consisted in intramuscular injection of 0·5 g. of streptomycin twice daily for 2 days, 0·4 g. twice daily for 2 more days, and then 0·2 g. twice daily for 2 or 3 days.

Diagnosis was confirmed by serial serological reactions (agglutination with tularaemin), in which the titre rose at the end of 3 weeks to two or three times that found in the initial stage of the disease, and much higher than that found in vaccinated persons. Unvaccinated persons show no agglutination for 14 or 15 days after infection; the subcutaneous allergy test, on the other hand, becomes positive between the 3rd and 5th days. The onset of the disease is acute. Case histories of 3 patients, representative of the three respiratory types, are reported; in all the patients recovery was complete.

L. Firman-Edwards

403. **" Coliform Diarrhoea " in Adult Hospital Patients**
W. McNAUGHT and J. S. STEVENSON. *British Medical Journal* [*Brit. med. J.*] **2**, 182–184, July 25, 1953. 6 refs.

The authors advance the view that in a certain number of cases the small localized outbreaks of diarrhoea which occur among adult hospital patients are due to type-specific strains of *Bacterium coli* of the types known to be closely associated with diarrhoea and vomiting in infants.

During the examination at Stobhill General Hospital, Glasgow, of 894 faecal specimens, mostly from cases of diarrhoea, type-specific strains were isolated from 15 patients. Brief case histories of these patients are given, and it is suggested that debility and general weakness are important predisposing factors, creating conditions for these strains to exert their pathogenic effects in the intestine. A third factor may be the virulence of the strain concerned. The preparation of the antisera and the bacteriological techniques used in the investigation are described. The strains isolated from the patients belonged to the O groups 111, 26, and 25. No organisms of the E group or Canioni strains were found.

R. B. Lucas

404. **Treatment of the Enteric Fevers with Synthomycin.** (Опыт лечения тифо-паратифозных заболеваний синтомицином)
T. K. NADZHMIDDINOV and E. C. SVESHNIKOVA. *Клиническая Медицина* [*Klin. Med.* (*Mosk.*)] **31**, 33–37, June, 1953. 2 figs.

The effect of synthomycin, an antibiotic used in the U.S.S.R., was tested in 40 cases of typhoid and paratyphoid fever occurring in 16 male and 24 female patients whose ages ranged from 4 to 50 years. The dosage in adults was 1 g. hourly for 2 hours, then 0·5 g. every 4 hours for 7 to 10 days, the total being 23 to 32 g. For children, 20 mg. per kg. body weight was given 4-hourly over the same period.

The results of this treatment were good, temperature falling by lysis beginning on the 3rd or 4th day of treatment Toxaemia rapidly abated, and the cerebral and cardiovascular complications common in these diseases did not occur. Synthomycin, however, did not prevent relapses, though these usually responded to a further course of the drug. The early appearance of an eosinophilia in the course of treatment was of good prognosis. Among side-effects observed were an allergic morbilliform rash, nausea, and vomiting.

(Klochina, discussing the same subject in another paper in the same journal (page 81), recommends a more prolonged course of treatment, lasting until the temperature has been normal for 10 days. Increasing the dosage does not prevent relapses. She appears to give half the dose in the afebrile stage, and points out that the disappearance of pyrexia and toxaemia does not necessarily indicate clinical or anatomical cure.)

L. Firman-Edwards

405. **Haemolytic Anaemia in Typhoid Fever. A Report of Six Cases, together with the Effect of Chloramphenicol and A.C.T.H.**
A. J. S. McFADZEAN and G. H. CHOA. *British Medical Journal* [*Brit. med. J.*] **2**, 360–366, Aug. 15, 1953. 6 figs., 25 refs.

Before 1945 the occurrence of haemolytic anaemia with haemoglobinuria as a complication of typhoid fever was rarely reported. Berman *et al.* (*Acta med. orient.* (*Tel-Aviv*), 1945, **4**, 175) found 9 cases of haemolytic anaemia of various degrees of severity in 152 cases of typhoid fever, and since then a few others have been reported. The diagnostic criteria are severe anaemia, an increase in the reticulocyte count, jaundice, and increased excretion of urobilinogen; in some cases there is haemoglobinuria.

The authors, from the University of Hong Kong, now report 6 cases in Chinese patients (4 males and 2 females) aged 19 to 38 years encountered in a consecutive series of 129 cases of *Salmonella typhi* infection. This is an incidence of 4·6%, which compares well with the incidence of 5·9% found by Berman. All the patients were jaundiced when admitted in the second week of the disease, and one had haemoglobinuria; otherwise the history was in no way different from that seen in uncomplicated typhoid. The haemoglobinaemia seemed to be closely associated with the typhoid infection. There was no evidence of exposure to toxic substances or ingestion of drugs recognized as causing haemolysis, jaundice, anaemia, or malnutrition. In 4 cases the condition cleared up spontaneously between the 23rd and the 28th days of the disease, irrespective of specific treatment of typhoid fever with chloramphenicol. In 2 cases, however, rapid improvement, in a matter of hours, followed intravenous administration of ACTH.

The pathogenesis of the haemolysis is obscure. It is suggested that an analogy may be found in the tendency to haemolytic anaemia observed, for example, in cases of chronic lymphatic leukaemia, Hodgkin's disease, reticulum-cell sarcoma, lymphosarcoma, and infectious mononucleosis. According to this, the haemolytic process would be associated with the hyperplasia of lymphoid and reticulo-endothelial tissue which occurs as an essential part of the pathology of typhoid fever, as also of the reticuloses.

H. Stanley Banks

Tuberculosis

406. **Studies on the Concentration of Streptomycin in the Treatment of Tuberculosis of the Joints.** [In English]
M. FELLÄNDER. *Acta orthopaedica Scandinavica* [*Acta orthop. scand.*] **22**, 283–294, 1953. 5 figs., 8 refs.

The concentration of streptomycin in the joint exudate in 9 cases of tuberculous synovitis was studied at St. Goran's Hospital, Stockholm, It was found that after intramuscular injection of 1 g. of streptomycin there was an effective bacteriostatic level in the joint exudate for 12 to 15 hours. When the same amount was injected into the affected knee-joint an effective level was maintained for 30 to 48 hours.

The author states that his treatment of cases of tuberculous synovitis is based on these findings—namely, 1 g. of streptomycin daily by intramuscular injection and 1 g. twice a week by intra-articular injection, the affected joint being immobilized in plaster of Paris. This treatment is continued for 6 weeks. [No details of results are given.] *L. W. Plewes*

407. **Effect of Streptomycin in Synovial Tuberculosis of the Knee**
W. S. SMITH and R. W. BAILEY. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **152**, 792–794, June 27, 1953. 6 refs.

In 5 cases (one in a child of 5) of proven synovial tuberculosis of the knee-joint, treatment with streptomycin was given (in 2 cases with PAS in addition) at the University Hospital, Ann Arbor, Michigan. On follow-up examination 3 to 6 years later no reactivation of infection and no development of bony or cartilaginous erosion was found in any case. [The series is too small and the follow-up period too short for any valid conclusion to be drawn.] *Norman Capener*

408. **Immunizing Properties of a Urea-killed Tubercle Vaccine**
C. N. ILAND. *Lancet* [*Lancet*] **2**, 277–279, Aug. 8, 1953. 6 refs.

In this preliminary communication the author, after discussing the advantages of using saturated urea as a killing agent, describes the immunizing properties of a urea-killed vaccine prepared in the Department of Preventive Medicine, University of Bristol, from a 4-week culture of virulent tubercle bacilli grown on Long's medium. The organisms were filtered, treated with an equal mass of urea, and the mixture kept for 4 days at 37° C. Twenty samples from 3 batches of vaccine were cultured on Löwenstein–Jensen medium and found to be sterile, and other samples inoculated into guinea-pigs did not produce any evidence of tuberculosis.

Two groups of guinea-pigs were then inoculated, one with the crude vaccine and the second with the killed cells after washing with phosphate buffer and resuspension in the same buffer. For each group there was an equal number of untreated controls, and all the animals were inoculated with virulent tubercle bacilli 30 days later. Both preparations gave a significant degree of protection. In another experiment one group of guinea-pigs received the urea-killed vaccine, one group was given B.C.G., and a third (control) group isotonic saline; 30 days later an injection of virulent tubercle bacilli was given. The urea-killed vaccine produced a higher degree of tuberculin-type hypersensitivity than did B.C.G., and when the animals were killed it was shown to have produced a degree of protection equal to, though not greater than, that given by B.C.G. Further investigations are in progress. *T. M. Pollock*

RESPIRATORY TUBERCULOSIS

409. **General Population Roentgenographic Surveys: Subsequent Course of Persons Considered to Have Tuberculosis**
W. R. AMES and M. H. SCHUCK. *American Review of Tuberculosis* [*Amer. Rev. Tuberc.*] **68**, 9–23, July, 1953. 2 figs., 14 refs.

Radiographic surveys of the population with a mobile 70-mm. photofluorographic unit were started by the Tuberculosis and Health Association of Buffalo and Erie County, New York State, in 1946, and a total of 330,585 films had been examined up to December, 1950. These gave some indication of the prevalence of pulmonary tuberculosis in the population, but left undiscovered the true incidence of the disease. Altogether, 976 persons examined were diagnosed as having pulmonary tuberculosis, of whom 656 had no previous knowledge that they were suffering from the disease. During a period of observation which varied from 6 months to 5 years, 23 of these 656 patients died from tuberculosis and 10 from other causes, while in 114 there was definite progression of the disease. Active disease was found most frequently in the younger age groups among the white population, the incidence declining with advancing age. The non-white population examined was too small for definite conclusions to be drawn on this point, though mortality from tuberculosis was about three times higher among the non-white than among the white patients *Franz Heimann*

410. **Correlation of Quantitative Mantoux Reactions with Clinical Progress in Pulmonary Tuberculosis**
H. M. TURNER. *Tubercle* [*Tubercle* (*Lond.*)] **34**, 155–163, June, 1953. 16 figs., 10 refs.

At the Sheffield Sanatoria and Clinic the relationship between the results of quantitative Mantoux tests and clinical progress in pulmonary tuberculosis was investigated. Patients were graded according to skin sensitivity as follows: Grade A, reaction of 12 mm. or more to

1 in 1,000,000 tuberculin; Grades B, C, and D, progressively decreasing allergic reactions; and Grade E, reaction of less than 8 mm. to 1 in 10,000 tuberculin. The author regards this grading as being convenient in clinical practice and reasonably accurate. He admits that hormonal factors influence the allergic state, but considers that any effect produced by them should not be regarded as a source of error. One example of the part played by endocrine factors is afforded by the changing allergic state during pregnancy in the patient whose tuberculous condition is quiescent.

A total of 191 patients in whom pulmonary tuberculosis was regarded as quiescent were followed up for 1 to 4 years. It was found that the majority of the 34 patients who had had a relapse belonged either to Grade E (58% relapse rate) or Grade A (44% relapse rate). Many of the patients in Grade A displayed the hyperallergic state only during or after the administration of antibiotics. In these cases there had usually been an atelectatic lobe with a cavity and a blocked bronchus, and hence absorption of tuberculous pus. The author regards the apparently quiescent case with Grade-A allergy with suspicion.

Two further groups of cases treated with streptomycin, in one of which the disease became quiescent while in the other it was fatal, were then studied. In the quiescent group increased allergy developed after streptomycin therapy (shift to Grades B and C), whereas in the fatal group the shift was far less pronounced, many patients remaining in Grade E.

The author concludes that the degree of allergy in a patient with pulmonary tuberculosis is not stable, and that the level of antigen production can be gauged by the Mantoux test. Active disease with low allergy might indicate an adverse antibody–antigen balance. Small lesions, such as those revealed on miniature radiographs, could be graded before and after a short course of treatment; the result might indicate whether the lesion was potentially unstable or not. He makes a plea for the use of quantitative Mantoux tests in clinical practice.

Paul B. Woolley

411. **Bacteriological Control of Therapeutic Trials in Pulmonary Tuberculosis**

P. COLLARD, K. ANDERSON, M. B. KING, D. G. CHALMERS, and R. KNOX. *Lancet* [*Lancet*] **2**, 155–158, July 25, 1953. 10 refs.

The authors discuss the value of bacteriological investigations during clinical trial of isoniazid, alone or in combination with other drugs, in fibrocaseous pulmonary tuberculosis (Joiner *et al.*, *Lancet*, 1952, **2**, 843, and 1953, **2**, 152). Specimens of sputum from 68 treated patients were examined, 1,727 of the specimens being examined by direct microscopy and 512 by culture and microscopy.

The authors state that to avoid false interpretations sputum should be examined frequently; over a given period the more frequent the examination, the higher the percentage of positive results obtained; " the fewer the examinations, the greater the apparent response ". The trend of the bacterial count is a reliable index of progress. For evaluating the different methods of treatment under trial, however, the proportion of patients with a negative sputum after treatment is a better guide than the mean count in the sputum. It is not always possible to obtain a culture after bacteria have been demonstrated by direct microscopy (culture rate 73% in treated patients and 91% in untreated patients). This may be due to three factors: (1) the bacteria may be dead; (2) they may be killed by the preliminary concentration; or (3) a sufficient amount of the drug may be carried over to the Löwenstein–Jensen slope to inhibit growth.

When the direct and indirect sensitivity tests were compared in 51 specimens it was found that the former was wasteful of media and the latter was slow. These are serious faults in trial work, and the authors prefer to rely upon the direct sputum count as an index of response to the drug. *T. Marmion*

412. **Antimicrobial Therapy of Pulmonary Tuberculosis: Review of Six Years' Experience at Fitzsimons Army Hospital**

C. W. TEMPEL, F. W. PITTS, and W. E. DYE. *Annals of Internal Medicine* [*Ann. intern. Med.*] **39**, 61–73, July, 1953. 13 refs.

The results of treatment of 875 cases of pulmonary tuberculosis with various antituberculous agents in " a methodical pattern of clinical investigation " at the Fitzsimons Army Hospital, Denver, Colorado, are reported. The drugs used were : streptomycin, PAS, thiacetazone, viomycin, terramycin, and isoniazid. Almost all the patients were young white adult males suffering from extensive caseous pneumonic tuberculosis with or without cavitation. The treatment and evaluation of results were carried out under standard conditions [for details of which, including the various dosage schedules used, the original paper should be consulted].

The most useful single drug was found to be streptomycin, which was equally effective whether given daily or every third day; in the latter case, however, the incidence of toxicity and of development of drug-resistance was reduced. Streptomycin was more effective when combined with any of the other drugs except thiacetazone, the best results being obtained with streptomycin given intermittently and PAS given daily. " Terramycin " and viomycin were found to be too toxic for routine administration, and their use had to be limited to those patients who could not tolerate other drugs. Preliminary results with isoniazid were very encouraging, but because of the rapid development of drug-resistance it should not be used alone. The combination of isoniazid with streptomycin gave results equal to or slightly better than those obtained with streptomycin and PAS, the speed with which sputum cultures became negative making it difficult to determine whether resistance developed to either drug. Thiacetazone was found to be of little use; maximal doses had some effect on the disease, but the incidence of toxic symptoms was high and resistant organisms appeared even when small doses (100 mg. daily) were used.

The authors conclude that, in general, chemotherapy should be continued up to 6 months after maximum

radiographic clearing has been obtained. It is the early case of tuberculosis (disease present less than one year) that derives most benefit from drug therapy, but these agents should not be regarded as the beginning and end of treatment, nor should they displace other non-chemotherapeutic measures of proven value. *T. Marmion*

413. ***para*-Aminosalicylic Acid in Sputum. Effect on Culture for Tubercle Bacilli**
B. FRUHLINGER and J. BALA. *American Review of Tuberculosis* [*Amer. Rev. Tuberc.*] **68**, 42–47, July, 1953. 2 refs.

The authors have been impressed by the increase, since the introduction of chemotherapy, in the number of cases in which sputum is reported as negative on culture although plenty of tubercle bacilli can be demonstrated to be present by microscopical examination of smears. This has been particularly noticeable in sputum from patients receiving a combination of streptomycin and PAS. At the Ray Brook State Tuberculosis Hospital, New York, therefore, 84 specimens of sputum from 59 patients receiving this treatment were examined by direct smear and by culture, and their content of PAS assessed.

The drug was found to be present in more than half of the cases—in concentrations of 0·03 mg. to 1 mg. per 100 ml. in 25 specimens, and in higher concentrations in 21 specimens. Among the 46 specimens which contained PAS were 29 in which the smear was positive for acid-fast bacilli, but 11 (38%) of these 29 were negative for tubercle bacilli on culture. Of 12 specimens of sputum which contained 1 mg. or more of PAS per 100 ml. and gave positive smears, 7 (58%) were negative on culture. The authors consider that the failure to culture tubercle bacilli can be largely accounted for by the presence of inhibitory concentrations of PAS in the sputum. The PAS, they consider, is derived from remnants of the drug left in the mouth after oral ingestion, and they suggest that the efficiency of the concentration culture method could be increased by proper cleansing of the mouth after taking PAS and by refraining from expectorating into the sample bottle until at least one hour has elapsed. *G. M. Little*

414. **A Clinical Evaluation of the Combination of Isoniazid with PAS in the Treatment of Pulmonary Tuberculosis.** (Vergleichende klinische Ergebnisse der Kombination INH+PAS bei Lungentuberkulose)
O. DÜGGELI and F. TRENDELENBURG. *Schweizerische medizinische Wochenschrift* [*Schweiz. med. Wschr.*] **83**, 600–602, June 27, 1953. 5 figs., 13 refs.

The authors compare the results obtained at the Wolfgang Sanatorium, Davos, in the treatment of pulmonary tuberculosis with isoniazid alone (35 cases) and in combination with PAS (28 cases) with those obtained with streptomycin and PAS (43 cases) after 3 months' observation. Assessment of the patient's progress was based on the erythrocyte sedimentation rate, the number of tubercle bacilli excreted (estimated by Gaffky's method), the general radiological appearances, and the extent of cavitation. It was found that treatment with isoniazid alone had a certain beneficial effect during the first 6 weeks, but that deterioration tended to occur between the 7th and 11th weeks owing to the rapid development of bacterial resistance to the drug. The combination of PAS with either streptomycin or isoniazid was more effective than isoniazid alone in all respects, and prevented the early development of drug resistance.
Franz Heimann

415. **Emergence of Bacterial Resistance in Pulmonary Tuberculosis under Treatment with Isoniazid, Streptomycin plus P.A.S., and Streptomycin plus Isoniazid. (M.R.C. Isoniazid Trial: Report No. 4)**
MEDICAL RESEARCH COUNCIL TUBERCULOSIS CHEMOTHERAPY TRIALS COMMITTEE. *Lancet* [*Lancet*] **2**, 217–223, Aug. 1, 1953. 13 refs.

The emergence of bacterial resistance was studied over a period of 6 months in more than 600 patients with pulmonary tuberculosis treated with: (1) isoniazid alone (H); (2) streptomycin with PAS (SP); or (3) streptomycin with isoniazid (SH). For the first 3 months the patients received the drugs in the following dosages: streptomycin 1 g. daily, isoniazid 100 mg. twice daily, and PAS (sodium salt) 5 g. 4 times a day. When chemotherapy was continued beyond 3 months the dose of streptomycin was usually 1 g. twice or 3 times a week. The numbers allocated to the three groups by random selection, were Group (H) 264; Group (SP) 233, and Group (SH) 130.

Isoniazid-sensitivity tests on positive cultures from patients in Group (H) revealed increased resistance in 64% at 3 months and in 93% at 6 months. Corresponding figures for patients in Group (SH) were 11% at 3 months and 50% at 6 months. It was found that over a period of 6 months streptomycin with isoniazid was as effective as streptomycin with PAS in preventing emergence of streptomycin-resistant strains.

In addition, it was revealed by this investigation that: (1) over a 3-month period after cessation of isoniazid therapy there was no evidence of any reversion of isoniazid-resistant strains either to a lower level of resistance or to sensitivity; and (2) where the organism was initially PAS-resistant no protection against the development of streptomycin-resistant strains was afforded by the combination of streptomycin with PAS.
R. H. J. Fanthorpe

416. **The Use of 4-Amino-4-β-hydroxyethylaminodiphenyl Sulfone (Hydroxyethyl Sulfone) in Pulmonary Tuberculosis**
H. M. PAYNE, R. L. HACKNEY, C. M. DOMON, E. E. MARSHALL, K. A. HARDEN, and O. D. TURNER. *American Review of Tuberculosis* [*Amer. Rev. Tuberc.*] **68**, 103–118, July, 1953. 9 figs., 2 refs.

A study was made at Howard University Medical School and Freedmen's Hospital, Washington, D.C., of the toxicity and effect on pulmonary tuberculosis of hydroxyethyl sulphone, a substance which was originally synthetized by Smith at the U.S. National Institutes of Health laboratories in 1948, as previously reported (Smith *et al.*, *Amer. Rev. Tuberc.*, 1949, **60**, 62; *Abstracts of World Medicine*, 1950, **7**, 328). Preliminary studies showed that toxicity of the drug is relatively low,

although one patient developed exfoliative dermatitis and severe jaundice, and another developed milder jaundice, but both recovered without any evidence of permanent liver damage. There was also some evidence that the substance has a depressive effect on erythropoiesis.

In the clinical trials on patients with advanced tuberculosis three groups of 57 patients each were treated respectively with (1) 1 g. of streptomycin daily for 90 days and 1·5 g. of hydroxyethyl sulphone daily for 180 days; (2) 1 g. of streptomycin alone daily for 90 days; and (3) 1 g. of streptomycin and 12 g. of sodium PAS daily for 90 days. Analysis of the results indicated that the combination of streptomycin with hydroxyethyl sulphone was more effective than streptomycin given alone, while continuation of the sulphone therapy in Group 1 prevented the spread of disease which occurred in the other groups on cessation of streptomycin therapy. There was also some evidence that the emergence of streptomycin-resistant strains was delayed in Group 1. Although hydroxyethyl sulphone given alone appeared to be effective against streptomycin-resistant strains in 4 cases, resistance of the tubercle bacillus to the sulphone was shown to appear after 3 to 4 months' treatment; it is therefore considered inadvisable to treat streptomycin-resistant cases with hydroxyethyl sulphone unless it can be combined effectively with another drug or drugs. *G. M. Little*

417. **A Comparative Study of Streptomycin and Dihydrostreptomycin in Pulmonary Tuberculosis**
S. C. F. Mahady, F. L. Armstrong, F. Beck, R. Horton, and N. S. Lincoln. *American Review of Tuberculosis* [*Amer. Rev. Tuberc.*] **68**, 238–248, Aug., 1953.

In a comparative study of streptomycin and dihydrostreptomycin, no difference in the therapeutic efficacy of the two drugs was discernible when they were administered for 120 days and when the results were evaluated at that time.

No significant difference was observed in the frequency of emergence of drug-resistant strains of tubercle bacilli which with either drug was less than 8%. The small percentage of patients in each original group who still had sputum positive for tubercle bacilli after one year of treatment emphasizes the impropriety of drawing any conclusions about the drug resistance studies with respect to the two drugs.

Ototoxicity of the two drugs is of considerable importance: Vestibular disturbances can occur with either drug but are more frequent, of greater severity, and often of earlier occurrence when streptomycin is employed than when dihydrostreptomycin is used. Auditory disturbances are relatively uncommon when streptomycin is employed and, when present, are usually of lesser severity. Auditory disturbances are more to be expected when dihydrostreptomycin is used. They are usually mild or slight in severity when drug therapy is given for only 120 days (or the equivalent). They are of greater severity and frequency when administration is prolonged beyond 6 months of daily treatment (or the equivalent). Furthermore, the auditory disturbances can progress even after therapy is stopped or they may appear some time after the conclusion of chemotherapy. The earliest changes of ototoxicity detected with either drug are usually tinnitus and/or high-tone loss of relatively mild degree.—[Authors' summary.]

418. **A Comparative Study of Streptomycin and Dihydrostreptomycin in Pulmonary Tuberculosis**
S. S. Cohen, L. Johnsen, M. R. Lichtenstein, and W. J. Lynch. *American Review of Tuberculosis* [*Amer. Rev. Tuberc.*] **68**, 229–237, Aug., 1953. 5 refs.

Both streptomycin and dihydrostreptomycin were shown to be valuable agents in the chemotherapy of amenable forms of tuberculosis in properly selected patients. It was not possible in the present study to determine any significant difference in the therapeutic efficacy of these two drugs. When administered in combination with *para*-aminosalicylic acid (or one of its salts), neither form of streptomycin was associated with the emergence of a significant incidence of drug-resistant infections.

Vestibular toxicity, which generally occurred relatively early in the course of treatment, was more frequently encountered with streptomycin. Auditory toxicity, which tended to occur relatively later, was more frequently due to dihydrostreptomycin. Although usually ranging from subclinical to moderate in degree, the auditory disturbance can be of serious proportions. It can be progressive or may appear belatedly after chemotherapy has ceased. High tone (audiometric) loss or complaint of sustained high-pitched tinnitus may represent the first indication of oncoming trouble and should always be considered significant.

Allergic responses to streptomycin were not infrequent and were occasionally severe. When dihydrostreptomycin was employed, however, allergic reactions were rarely encountered.—[Authors' summary.]

419. **A Clinical and Endoscopic Study of Bronchial Reactions in the Course of Pulmonary Tuberculosis in the Adult.** (Étude clinique et endoscopique des réactions bronchiques au cours de la tuberculose pulmonaire commune de l'adulte)
G. Brouet, P. Y. Paley, J. Marche, L. Sang, J. Chrétien, and R. Gérard-Marchant. *Revue de la tuberculose* [*Rev. Tuberc. (Paris)*] **17**, 452–467, 1953. 6 figs.

The authors examined bronchoscopically 200 unselected patients (100 men and 100 women) with pulmonary tuberculosis in order to study the frequency and importance of bronchial involvement. In the majority of cases the procedure was repeated some weeks later to assess the effect of therapy. Biopsy was performed in 57 cases; the site was invariably found to have healed on re-inspection. In no case was there any spread of disease attributable to the bronchoscopy.

Abnormal appearances were encountered in 144 cases, but in 6 cases only were these specifically tuberculous, that is, ulceration or granulations. In the remainder the findings consisted mainly in oedema, redness, hypersecretion, and erosions which bled on contact. The bronchi of the upper and dorsal lobes

were the most frequently affected. Bronchial stenosis inevitably occurs in some degree, and is most marked at sites of branching as the result of inflammatory swelling of the secondary carinae; it is reversible at first, but may become permanent later if scarring occurs. In the great majority of the present cases the stenosis was due to mucosal oedema and tenacious muco-pus, and disappeared completely with chemotherapy. In 3 cases, however, cicatricial changes were seen which were clearly irreversible. Bronchial calibre was regarded as normal in 79 cases; of the remainder the stenosis was considered mild in 20, moderate in 66, and severe in 35 cases. The biopsy specimens showed typical giant-cell systems in 8 cases, and in 26 others showed lymphocytic infiltration.

There was little correlation between clinical and radiological findings and the extent of bronchial disease. In the cases re-examined, resolution of the bronchial inflammation ran parallel with radiological improvement, but occasionally lagged behind. The authors consider that preliminary bronchoscopy is essential before deciding on the induction of artificial pneumothorax. *D. Weitzman*

420. **Pulmonary Function and Circulatory Dynamics in Artificial Pneumoperitoneum. I. Studies on Patients with Pneumoperitoneum Therapy for Pulmonary Tuberculosis**
R. C. KORY, D. C. ROEHM, G. R. MENEELY, and R. A. GOODWIN. *Diseases of the Chest* [*Dis. Chest*] **23**, 595–607, June, 1953. 3 figs., 25 refs.

Since little has so far been done to ascertain the effects of pneumoperitoneum on the respiratory and cardiovascular systems, the authors undertook the present study, which was carried out at Thayer Veterans Administration Hospital and Vanderbilt University School of Medicine, Nashville, Tennessee, on 5 male patients with pulmonary tuberculosis. Clinical details of each case are given. Direct spirography was used to determine the vital capacity, while the maximum breathing capacity was determined with a Tissot spirometer and the other gaseous exchange values by well-established methods. The pressure in the systemic and pulmonary circulations was ascertained by Cournand's technique of cardiac catheterization, and cardiac output by the direct Fick method; samples of arterial and mixed venous blood were also analysed. From these findings other values, such as total peripheral resistance and pulmonary resistance, could then be calculated. In 4 of the patients the pneumoperitoneum refill was postponed, and when only a trace of air remained the maximum breathing capacity, dead space, and lung volume were determined and cardiac catheterization carried out. The pneumoperitoneum was then refilled to its former pressure and the values determined again. In the fifth patient determinations were first made with the pneumoperitoneum filled, and repeated 1 month later when it had been abandoned.

There was a slight decrease in total capacity in all 5 patients and a relatively greater decrease in residual air. The vital capacity and dead space scarcely changed, but there was a moderate decrease in maximum breathing capacity. The arterial O_2 and CO_2 content varied very little, and cardiac output fell slightly in 4 patients. Pressure in the pulmonary capillaries, right heart, and iliac veins was virtually unchanged. It is concluded that the fall in total capacity was due mainly to reduction in residual air. In contradistinction to certain previous reports, but in agreement with recent work, vital capacity was not impaired. The authors conclude that pneumoperitoneum in pulmonary tuberculosis has little effect on cardiac and pulmonary function. *Paul B. Woolley*

421. **The Significance of Upper Lobe Atelectasis during Artificial Pneumothorax**
G. L. BRINKMAN. *British Journal of Tuberculosis and Diseases of the Chest* [*Brit. J. Tuberc.*] **47**, 131–134, July, 1953. 8 refs.

In an attempt to resolve the conflict of views on the danger of the development of atelectasis in patients with artificial pneumothorax, the author, working at the Cashmere Sanatorium, New Zealand, investigated 358 patients in whom artificial pneumothorax had been maintained for at least 3 months during the period 1939 to 1948 and who had not received any specific antibiotics. Of this number, 49 patients developed upper-lobe atelectasis; of these, 19 progressed to massive collapse and were excluded from the study, leaving 13 patients who had collapse of the right upper lobe and 17 with left upper-lobe involvement.

In discussing the factors predisposing to this complication the author concludes that the most important are the presence of toxaemia at the time of induction (as judged by the temperature and erythrocyte sedimentation rate) and a solitary " tension " cavity in the upper lobe. Other factors are the presence of a heavy root shadow in the pre-induction radiograph and the persistence of fluid; an effusion had been present at some period in approximately half the patients developing atelectasis compared with only 16% of the remainder. The shape of the atelectasis on the radiograph did not help in assessing prognosis. At the end of 6 years 48% of patients in the atelectatic group were dead compared with 25% of non-atelectatic patients. It is clear that this complication gravely affects the prognosis.
Paul B. Woolley

422. **The Early Results of Resection for Pulmonary Tuberculosis**
J. DARK and P. JEWSBURY. *Lancet* [*Lancet*] **2**, 64–66, July 11, 1953. 15 refs.

The management of, and early results in, 141 cases of pulmonary tuberculosis treated by resection by the Manchester Region Thoracic Surgical Units between May, 1949, and April, 1952, are reviewed.

Of the 141 patients, 44 were males and 97 females, and two-thirds were in the age group 20 to 40 years. The indications for operation were as follows: destroyed lung (56), multiple cavities (17), upper-lobe cavities (32), lower-lobe cavities (25), tuberculoma (8), bronchiectasis (2), empyema (2). Of the 73 cases in the first two groups 10 were complicated by empyema; 10 cases in the series came under the heading of " failed thoracoplasty ".

In all but one case streptomycin and PAS were given 2 to 3 weeks before operation and for 3 months afterwards. Where adhesions were found the lung was freed in the extrapleural plane; bronchial stumps were closed by interrupted, over-the-end, nylon or linen-thread sutures. The procedures carried out were: pneumonectomy (41 right and 44 left), lobectomy (50), and segmental resection (7); there was one case of bilateral resection. Thoracoplasty was performed in addition on 8 of the 25 patients undergoing upper lobectomy and on 62 of the 85 undergoing pneumonectomy (in most instances subsequently).

There were 11 deaths in the series, 5 due to the operation, 5 to bronchopleural fistula, and 1 to empyema and spread. The complications were: reactivation of the disease in 11 cases (contralateral 6, ipsilateral 5); bronchopleural fistula in 12; tuberculous empyema in 3; and tuberculous wound infection in 2. There was no reactivation in the lower lobe in the 10 cases of upper lobectomy in which space-reducing measures were carried out (thoracoplasty in 8 and phrenic paralysis in 2), but ipsilateral reactivation was found in 3 of the remaining 15 cases without space-reduction. Phrenic crush was carried out at the same time as lower lobectomy in 13 cases and in none of these was there ipsilateral reactivation, whereas this complication was seen in 2 of the 11 cases without phrenic paralysis. There were 4 cases of reactivation after pneumonectomy (in 2 after subsequent thoracoplasty and in 2 secondary to bronchopleural fistula). No reactivation of the disease was found in the 23 patients undergoing pneumonectomy without thoracoplasty.

Bronchopleural fistula occurred in 12 cases, 5 being fatal; in 2 cases the fistula was closed by thoracoplasty, but in the remaining 5 it persisted. Fistulae were commoner among patients who had had streptomycin therapy than among those who had not. The results of pleuropneumonectomy for tuberculous empyema were disappointing; of 11 patients 4 died, only 4 being cured.

The follow-up period in some cases was 6 months, but 94 of the 130 survivors had been followed up for more than one year. In 119 patients the disease was quiescent, 60 of them being able to work full-time. A complaint of severe dyspnoea was made by 15 of the 75 patients who survived pneumonectomy; on 14 of these thoracoplasty had also been performed.

The value of space-reduction is discussed, the authors concluding that this procedure is desirable after lobectomy and segmental resection, but is neither necessary nor desirable after pneumonectomy.

F. J. Sambrook Gowar

423. **Results of Thoracoplasty. Follow-up of 583 Patients**

R. LAIRD. *Lancet* [*Lancet*] **2**, 319–322, Aug. 15, 1953. 10 refs.

A standard 2- or 3-stage thoracoplasty with apicolysis was carried out on 583 patients at Clare Hall Hospital, South Mimms, Herts., during the period 1944–50, and in this paper the author reviews the results. Altogether 569 patients were able to leave hospital; at the time the patients were discharged the sputum was negative in 435 and positive, though there was clinical improvement, in 122, while in 12 there was active disease. Follow-up examination of the 525 who were traced revealed that in 73 of the 122 with a positive sputum on discharge the disease had remained quiescent.

Of 251 patients in the series on whom a 5-year follow-up investigation was possible, 222 were alive, the disease being quiescent in 181. Several interesting aspects of thoracoplasty—namely, anaesthesia, associated non-tuberculous conditions, scoliosis, age in relation to operation, postoperative spread, and contralateral pneumothorax—are discussed. *R. L. Hurt*

424. **"Blocked Cavities."** (Les "cavernes pleines")

A. BERNOU, J. TRICOIRE, and J. TOURNIER. *Presse médicale* [*Presse méd.*] **61**, 883–884, June 20, 1953. 7 refs.

The authors present a study of 176 cases of "blocked cavity", in 54 of which (31·5%) the cavity re-opened at a later date. As the authors have previously pointed out (*Rev. Tuberc.* (*Paris*), 1947, **11**, 10) the healing of these cavities may take place by one of two methods: (1) by the accumulation of fluid which gradually fills up the cavity in consequence of a partial or total obstruction of the bronchus, or (2) by the walls of the cavity progressively thickening centripetally in all parts of its circumference. In cases of the first type re-opening of the cavity is probably due to recanalization of the healed bronchus, and is more frequent when the obstructed bronchus is large and filled with caseous material.

Of the 54 cavities which re-opened, 22 closed spontaneously with rest, without any bronchogenic spread; in 16 other cases the cavity was closed by collapse therapy, and again there was no evidence of spread. [The fate of the remaining cases is not at all clear.] Most of the bad results were in cases, many fatal, in which the condition was bilateral and was only one of several pathological elements present. The authors found that the adverse effect of the re-opening of a cavity on the long-term prognosis was much less than they had feared. It appears that prolonged obstruction of the bronchus reduces the pathogenicity of the tubercle bacilli in the cavity, and it is possible that prolonged administration of antibiotics also favours the apparent sterilization.

G. M. Little

425. **Tuberculoma of the Lung.** (Das Tuberkulom der Lunge)

A. RÜTTIMANN and F. SUTER. *Schweizerische medizinische Wochenschrift* [*Schweiz. med. Wschr.*] **83**, 591–600, June 27, 1953. 34 figs., 30 refs.

The authors define a tuberculoma of the lung as a more or less round, well-defined, and frequently solitary lesion 1 to 6 cm. in diameter, which must be distinguished from a primary tuberculous lesion, an inspissated cavity, and a localized area of caseous pneumonia. The histology of a tuberculoma is essentially the same as that of any other form of tuberculosis, having the appearance of an encapsulated focus of tuberculous pneumonia slowly progressing and increasing in size, usually concentrically. Staining for elastic fibres may reveal large portions of

intact lung structure of which there is no evidence in an inspissated cavity. This paper is based on the authors' findings in more than 8,000 cases of pulmonary tuberculosis examined radiologically at sanatoria in Davos between 1930 and 1952, amongst which they discovered 87 tuberculomata in 77 cases (0·96%). They are, however, of the opinion that the true incidence probably amounted to about 2 or 3%, improvements in radiological diagnosis having now made it possible to detect cases which would have been missed in the early part of the period under review. The segmental distribution of the tuberculomata was preponderantly in the upper lobes (69%). The average age of the patients was 26 years, the youngest being 16 and the oldest 54, and the majority of patients were between the ages of 20 and 35. After 1 to 10 years' surveillance the disease was healed in 11 cases, remained stationary in 36, and showed evidence of activity—enlargement, spread of infection, or cavitation—in 40. The main problem of diagnosis is to differentiate the round *x*-ray shadow of the tuberculoma from that due to a benign or malignant growth or an inspissated cavity. The finding of tubercle bacilli is essential for diagnosis. Treatment in the cases reported consisted in rest, alone or in combination with antibiotics and pneumothorax; in cases where conservative methods fail the authors recommend resection

Franz Heimann

426. **"Tuberculoma" of the Lung and Rounded Infiltrations of Tuberculous Origin.** (Considerazioni sul così detto tubercoloma del polmone e sull'infiltrato rotondo di natura tubercolare)
F. Nobile and A. Montanari. *Rivista di patologia e clinica della tubercolosi* [*Riv. Patol. Clin. Tuberc.*] **26**, 273–292. Sept.–Oct., 1953. 22 figs., bibliography.

TUBERCULOUS MENINGITIS

427. **The Early Diagnosis of Tuberculous Meningitis with "Uranin" (Sodium Fluorescein).** (Zur Frühdiagnostik der tuberkulösen Meningitis mit Uranin (Fluorescein-Natrium)
R. Fujii and F. Sakata. *Zeitschrift für Kinderheilkunde* [*Z. Kinderheilk.*] **73**, 1–7, 1953. 10 refs.

In children with tuberculous meningitis the permeability of the meninges to "uranin" (sodium fluorescein) varies with the course of the disease, changes in permeability preceding other cerebrospinal-fluid changes and their demonstration thus providing means of early diagnosis. For this purpose 0·3 ml. of 10% uranin solution per kg. body weight is injected intramuscularly and its concentration in the cerebrospinal fluid estimated after 3 hours by measurement of the fluorescence of the fluid in ultraviolet light. The value in normal infants of less than 3 months is 0·03 to 0·04 mg. per 100 ml., and in those over 1 year 0·02 mg. per 100 ml.

At the Paediatric Clinic of Tokyo University the uranin test was performed in 49 cases of tuberculous meningitis in children, and a raised value was found in all cases. In those cases in which the value was as high as 0·5 mg. per 100 ml. before or during treatment the prognosis was bad and there was a tendency to relapse even if the cerebrospinal fluid became normal in other respects. Continuation of streptomycin therapy is therefore advisable until the uranin value is less than 0·03 mg. per 100 ml. Of 21 children with miliary tuberculosis, in 12 the uranin value was increased; 3 of these died and 3 others developed meningitis: it was found possible to predict the onset of meningitis in these cases 1 to 2 months before clinical or cerebrospinal-fluid changes appeared. Of 102 cases of pulmonary tuberculosis in children, in 8 there was increased permeability to uranin. These were treated with streptomycin as incipient cases of meningitis, upon which the uranin value became normal. Except for a yellow discoloration of the skin, no side-effects have been observed following the injection of uranin.

Athel Hockey

428. **The Electroencephalogram in Children with Tuberculous Meningitis.** (Étude de l'électroencéphalogramme dans la méningite tuberculeuse de l'enfant)
P. Laget, C. Bach, C. Alufi, and R. A. Marquézy. *Presse médicale* [*Presse méd.*] **61**, 984–987, July 8, 1953. 10 figs., 11 refs.

A total of 408 electroencephalograms (EEGs) from 59 children treated for tuberculous meningitis at the Hôpital Trousseau, Paris, are analysed and discussed. In 47 cases the initial record was made at the beginning of treatment and follow-up records were obtained at intervals for many months after the clinical recovery. The authors follow the classification of Debré in dividing the tracings into four groups: (1) those showing some isolated slow waves; (2) with more numerous bursts of slow waves; (3) showing very frequent slow waves, with an almost complete disappearance of background activity; and (4) completely disorganized. To these they add three further groups: (5) an extremely flat record, which is of very serious prognosis; (6) high-voltage, sharp waves at 8 to 10 c.p.s. on a background of slow activity, also found in serious cases; and (7) high-voltage fast activity at 25 c.p.s., found in 3 patients, 2 of whom had a marked residual hydrocephalus.

Contrary to the opinion of Chaptal the authors do not consider a posterior localization of the abnormalities to be an indication of basal involvement and a serious prognosis. Foci were rare in their cases and lateralization suggested by the EEG findings did not constantly correspond to the lateralization suggested by clinical findings. Very abnormal initial records are considered to be of serious prognosis, but the evaluation seems to depend on the treatment given; there was rapid clinical recovery and improvement in the EEG in 4 children treated with isoniazid associated with streptomycin and PAS, despite the presence of gross abnormalities in the initial tracing. The authors find that as a general rule changes in the EEG tend to follow changes in the clinical condition, so that relapses cannot be foreseen by means of the EEG. Mild changes in the EEG persisted in more than half of the patients after clinical recovery, but tended to disappear after a few months.

W. A. Cobb

Venereal Diseases

429. **A Comparison of the Neurath and *Treponema pallidum* Immobilization Procedures**
A. N. Roy, J. H. Hill, J. L. Gowdey, L. C. Kelcec, and C. R. Rein. *American Journal of Syphilis, Gonorrhea and Venereal Diseases* [*Amer. J. Syph.*] **37**, 338–343, July, 1953. 9 refs.

Before the development of the treponema immobilization (T.P.I.) test the euglobulin-inhibition or Neurath test provided one of the few possible laboratory controls for standard serum tests for syphilis. According to Neurath, biological false positive reactions may be differentiated from true syphilitic reactions by means of a heat-stable serum component or "inhibitor". This substance inhibits the serological activity of globulin fractions of biological false positive sera, but does not appreciably affect the same fractions of syphilitic sera. The results of the Neurath test and the T.P.I. test were therefore compared with each other and with the clinical diagnosis in a series of 96 patients at the New York University–Bellevue Medical Center, New York.

Complete agreement between the two tests was noted in 65 cases (67·7%) and disagreement in 11, while in 20 cases the Neurath test was inconclusive or showed specimen-to-specimen variation, whereas the T.P.I. test was conclusive and reproducible. The T.P.I. test was in agreement with the clinical diagnosis in 95·7% (89 out of 93 cases) but the Neurath test in only 64·5% (60 cases). In 7 cases of pityriasis rosea the result of the T.P.I. test was negative in all cases, whereas the Neurath test result was negative in 3 and of the biological type in 4. The T.P.I. test was negative in 6 patients with lupus erythematosus, while the Neurath test was negative in 2, of biological type in 2, and gave a variable result in the 2 others. *R. R. Willcox*

430. **Observations on the Optimal Zone Reaction and Seroresistance**
G. R. Cannefax. *American Journal of Syphilis, Gonorrhea and Venereal Diseases* [*Amer. J. Syph.*] **37**, 344–347, July, 1953. 3 figs., 1 ref.

The optimal-zone procedure was performed in 300 seroresistant cases of syphilis at the U.S. Public Health Services Treatment Center for Venereal Diseases at Hot Springs, Arkansas. In this test the flocculation obtained with serum and antigen in different proportions is recorded in sequence of increasing serum:antigen ratio, producing a so-called pattern. Kahn has suggested that certain post-treatment patterns may have possible prognostic significance—for example, in the early determination of ultimate seroresistance following presumably adequate therapy.

When the results of the optimal-zone procedure were compared with the reagin titre in this series it became increasingly evident that the optimal-zone patterns were predominantly dependent upon reagin concentration. It is considered, therefore, that the optimal-zone procedure does not produce information concerning seroresistance that is not already obtainable with the more easily performed standard serological tests for syphilis provided these are performed at regular intervals. *R. R. Willcox*

431. **The Treatment of Gonorrhoea by the Oral Administration of "Leukomycin" [Chloramphenicol].** (Zur Behandlung der Gonorrhoe unter Berücksichtigung des peroral verabreichbaren Mittels Leukomycin)
R. Brett. *Dermatologische Wochenschrift* [*Derm. Wschr.*] **128**, 1141–1144, 1953. 4 refs.

For the treatment of early gonorrhoea penicillin has certain disadvantages and dangers, which are accentuated in the absence of adequate laboratory facilities. Since such treatment is now undertaken largely by the general practitioner, there is a need for an equally effective drug which is less liable to suppress the early signs of a concomitant syphilitic infection and to induce drug-resistance in the organism and hypersensitivity in the patient.

Chloramphenicol has been reported to possess these properties in some degree, and has the added advantage or being effective when given by mouth. The author therefore undertook preliminary trials with the German equivalent, "leukomycin", in 30 female patients with untreated urethral, cervical, or rectal gonorrhoea at the Skin Clinic of the University of Mainz. Leukomycin was given in doses of 0·25 g. at intervals of 3 to 4 hours, 2, 3, and 4 doses being given in different cases selected at random. Smears of the discharge were examined daily for the first 10 days, and the patients subsequently remained under surveillance at the clinic for an unspecified period. In the one case in which the drug caused a severe gastro-intestinal disturbance the smears remained positive, and in another case gonococci returned after the patient's discharge from hospital, probably as a result of reinfection. The remaining 28 patients were cured. A further trial was then carried out in which 40 female patients were given 2 doses of 0·25 g. at an interval of one hour and smears were examined at frequent intervals after the second dose. In every case gonococci had disappeared within 3 to 4 hours, not even degenerate forms being visible.

The author concludes that leukomycin by mouth is effective against gonorrhoea in the female in lower dosage than has hitherto been recommended for chloramphenicol, and considers that if this is confirmed in the male there is a good case for its general use in place of penicillin. *Donald Crowther*

See also Chemotherapy, Abstract 384.

Tropical Medicine

432. An Evaluation of New Treatments and Other Factors in Leprosy

W. S. DAVIDSON. *Leprosy Review* [*Leprosy Rev.*] **24**, 139–146, July, 1953.

The author compares the results of 5 different schedules of treatment employed in 121 cases of lepromatous leprosy at the Derby Leprosarium, Western Australia. The schedules were: (1) " sulphetrone " (solapsone) given intramuscularly in doses of 4 ml. of a 50% solution twice a week, the full dose being reached in 4 weeks (43 cases); (2) solapsone by mouth, 3 g. daily, the full dose being reached within 3 months (17 cases); (3) dapsone (DADPS), 200 mg. intramuscularly daily, the full dose being reached in 2 months (33 cases); (4) " neustab " (thiacetazone), of which 25 mg. was given daily during the first month, 50 mg. daily from the 2nd to the 7th months, increasing to 200 mg. daily from the 8th to the 12th months (20 cases); and (5) thiacetazone, starting with the same dose as in Schedule 4, but increasing it more rapidly and reaching the full dose of 200 mg. daily in 3 months (8 cases only). All treatments were continued for one year; in Schedules 2, 3, and 5 one rest day was given every week and one week's rest every 2 months.

Treatment with 200 mg. of thiacetazone daily gave the best results, although this drug in low dosage was ineffective. With intramuscular injections of solapsone and dapsone the results were about equal, and less good than with thiacetazone. Solapsone was the least toxic and thiacetazone the most toxic of the substances tested. Solapsone given orally gave comparatively poor results owing largely to a fall in the haemoglobin level, a similar fall occurring in those failing to respond to thiacetazone. The author found that to obtain the best results a haemoglobin value of not less than 13 mg. per 100 ml. is necessary, and that underdosage was associated more frequently with a fall in haemoglobin value than was full dosage. No significant differences in improvement were noted between the various types of leprosy, between lepromin-positive and lepromin-negative cases, or between those with lepra reactions and those without.

R. R. Willcox

433. Report on 9 Months Treatment of Leprosy with Isoniazid (" Nydrazid ")

F. LATAPI, J. BARBA RUBIO, O. RODRIGUEZ, and S. CASTRO ESTRADA. *Journal of Investigative Dermatology* [*J. invest. Derm.*] **21**, 27–35, July, 1953. 5 figs., 17 refs.

A preliminary report is presented on the treatment of leprosy with isoniazid at centres in Mexico City and Guadalajara, 14 patients (9 male and 5 female) ranging in age from 14 to 25 years having been treated over a period of 9 months. The type of disease was lepromatous in 13 cases and tuberculoid in one, 3 of the former being incipient and 10 moderately advanced and the tuberculoid case being an early one; all except the last were bacteriologically positive at the outset, and most had had some sulphone treatment previously. The dosage of isoniazid employed was 3 to 5 mg. per kg. body weight daily; it was well tolerated and produced mild lepra reactions in only about half the cases treated.

In all the lepromatous cases a reduction in the degree of cutaneous infiltration and in the number and size of the nodules was noted, the nodules almost disappearing in some cases, and similar improvement was observed in the lesions of the nasal mucosa and conjunctiva. Serial biopsies revealed a progressive reduction in number of, and degenerative changes in, the *Mycobacteria leprae* in stained specimens. With one exception, no new lesions appeared in the lepromatous cases while under treatment; in the exceptional case the disease flared up after 4 months' treatment during which the lesion had practically disappeared, and new lesions presenting a mixed lepromatous and tuberculoid histological picture developed in addition to the reactivation of old lesions. No change was seen in the one tuberculoid case.

No controls undergoing sulphone treatment were available, but the authors consider that further studies are justified.

Clement Chesterman

434. Use and Effectiveness of Anti-malarial Drugs. Experience of Non-native Resident Population of Nigeria, West Africa

B. M. NICOL. *British Medical Journal* [*Brit. med. J.*] **2**, 177–180, July 25, 1953. 12 refs.

The efficacy of the antimalarial drugs in common use for the prevention of malaria in Nigeria was assessed in an investigation carried out on all non-native adults and children attending the author's out-patient clinic at the Creek Hospital, Lagos, during a period of 17 months in 1951–2. The population thus studied consisted of 441 adults and 90 children, 456 of whom were taking some antimalarial drug regularly. Thick blood films were examined for parasites in all cases of pyrexia or other clinical finding suggestive of malaria, a diagnosis of " clinical malaria " being made if there was a suggestive history of periodic fever and response to specific treatment even though the blood findings were negative.

The over-all incidence of malaria among those regularly taking prophylactic drugs was 8%. It was found that many patients who had formerly taken quinine or mepacrine had now changed to one of the newer preparations; of those who had relinquished quinine, 80% gave as their reason the failure of quinine to prevent frequent attacks of fever, whereas in the case of mepacrine the reason given for the change in 89% of cases was the yellow staining of the skin. In low dosage—100 mg. daily—proguanil had failed to prevent fever in some cases and had consequently been abandoned by a few patients, but never because of anorexia or other side-effects; a change

to higher dosage—200 mg.—of the same drug, however, gave satisfactory results. Only 16% of the group were taking quinine and 5% mepacrine. The majority (68%) were taking proguanil (100 or 200 mg. daily) which, together with chloroquine (300 mg. twice or thrice weekly), appeared to be completely effective, the patients concerned showing no overt malaria and complaining of no such untoward symptoms as occurred with quinine and mepacrine. The author states his preference for proguanil in doses ranging from 50 mg. daily for infants under 1 year to 200 mg. daily for adults.

William Hughes

435. **Pyrimethamine ("Daraprim") in the Treatment of Vivax Malaria**

G. COVELL, P. G. SHUTE, and M. MARYON. *British Medical Journal* [*Brit. med. J.*] **2**, 258–259, Aug. 1, 1953.

Twelve patients suffering from primary attacks of mosquito-induced vivax malaria (Madagascar strain) were treated with 50 mg. of pyrimethamine daily for five days. The clinical response to the action of the drug was slow, and for this reason alone we regard it as unsuitable for treatment of the clinical attack in non-immune subjects.

Four of the patients relapsed between the 55th and 99th days after completing the course, one of them on two occasions. On the 99th day 11 of the group were given a single dose of 25 mg. of pyrimethamine, which was repeated at weekly intervals for the following seven weeks. All of them relapsed on one or more occasions between the 8th and 18th weeks after completing this eight-weeks course.

There is no indication that either of the two courses of pyrimethamine administered in this trial (50 mg. daily for five days during the primary attack and 25 mg. weekly for eight weeks, starting three and a half months later) were of any value in preventing the incidence of relapse, though it is possible that the attacks might have occurred somewhat earlier had the drug not been given.—[Authors' summary.]

436. **An Experiment in the Control of Malaria and Bilharziasis**

W. ALVES and D. M. BLAIR. *Transactions of the Royal Society of Tropical Medicine and Hygiene* [*Trans. roy. Soc. trop. Med. Hyg.*] **47**, 299–308, July, 1953. 6 refs.

In Southern Rhodesia malaria is spread by *Anopheles gambiae* in the rainy season (from October to May), the annual epidemic lasting for about 5 months, while bilharziasis, though endemic, is probably spread chiefly during the dry season. Malaria control is of considerable economic importance; it has happened in past years that good rains have produced bumper crops in the native reserves, but the population was too ill with malaria to reap them. Moreover, the greater part of the native population is infected with bilharziasis.

It was therefore decided by the Southern Rhodesia Health Department to establish one organization to deal with both diseases, 6 field units being formed, each with a staff of 10 Africans and 1 European supervisor, to cover 13 native reserves with a total population of more than 200,000. During the first 3 months of the rainy season the interiors of all dwellings are sprayed with benzene hexachloride (BHC) in a concentration of 33 to 40 mg. per square foot (350 to 425 mg. per sq. metre) of surface sprayed, and the spraying is then repeated, if possible during the second 3 months. An average of 180 huts can be sprayed by one unit in a day, at an estimated cost of 3*s.* 1*d.* per hut, or 1*s.* 8*d.* per head of population. The anti-bilharziasis work, which occupies the units during the dry season, consists in spraying rivers and streams with copper sulphate solution to achieve a concentration of about 10 to 30 parts per million, which kills not only the snails, but also the young fish; however, fish are not at present important as native food. The cost of this work is about £2,000 per unit, or about 1*s.* per head of population.

Examination of the blood of 156 children in 1948 (before spraying was started) showed that 112 (71·8%) were infected with *Plasmodium falciparum*; in 1950, 28 out of 92 children in the same reserve (30·4%) were infected, and in 1952 only 5 out of 106 children (4·7%) were infected. Similar results were obtained in other reserves. The effect of the anti-bilharziasis work cannot be judged for at least 5 years. *J. F. Corson*

437. **Scorpion Toxin and Antagonistic Drugs**

H. ROHAYEM. *Journal of Tropical Medicine and Hygiene* [*J. trop. Med. Hyg.*] **56**, 150–158, July, 1953. 25 refs.

After discussing the literature on the action of scorpion toxin the author describes the physical and chemical properties of the toxin and methods of preparation and standardization.

At Kasr El-Aini, Cairo, experimental work was carried out on dogs to determine the action of the toxin on the autonomic nervous system. It was found that doses of 0·015 to 0·15 mg. per kg. body weight injected intravenously produced intermittent rise and fall in blood pressure due to stimulation of both the sympathetic and the parasympathetic nervous systems. When 0·15 mg. of atropine per kg. body weight was injected there was a very definite rise in blood pressure. In other experiments, 5 mg. of hexamethonium bromide per kg. body weight was given intravenously so as to block all the ganglia; after the scorpion toxin had been administered much the same effects on the blood pressure were observed.

In the course of this work various drugs expected to be protective against scorpion toxin were tested, the drugs being ergotoxin, atropine, and "regitine" an active synthetic sympathicolytic drug related to tolazoline. Rats, each weighing 100 g., received a subcutaneous injection of 1 M.L.D. of scorpion toxin. In addition they received, singly, in various combinations, or all together, 0·05 mg. of ergotoxin per kg. body weight, 0·05 mg. regitine per kg., 1·6 mg. of atropine, and 0·1 ml. of antitoxic serum. The number of deaths in each group within 5 hours was noted. Complete protection was obtained when all four were given together [but it is difficult to determine which was the most effective singly. A clinical trial is suggested]. *H. David Friedberg*

Allergy

438. **The Circulating Eosinophil Cells in Hay-fever Patients in Relation to Specific Desensitization.** [In English]
P. J. DRAGSTED. *Acta allergologica* [*Acta allerg. (Kbh.)*] **6**, 103–106, 1953. 1 ref.

At the Copenhagen Hospital, Hellerup, the number of eosinophils in the blood of 24 patients suffering from hay-fever was studied before and after exposure to a specific antigen. Of the 24 patients, 11 had not previously received treatment for hay-fever, while 13 had received injections of pollen extract for at least one year. When both groups were exposed to a specific antigen it was found that in the 11 untreated patients there was a rise in the number of eosinophils per c.mm. averaging 46% of the initial count. In the 13 treated patients there was a fall in the eosinophil count averaging 51% of the initial value. *A. W. Frankland*

439. **The Treatment of Ragweed Hay Fever**
C. J. MALLOY. *Canadian Medical Association Journal* [*Canad. med. Ass. J.*] **68**, 583–587, June, 1953. 1 fig., 36 refs.

Methods of treatment of ragweed hay-fever are discussed and the results obtained at the Royal Victoria Hospital (McGill University), Montreal, in 78 cases with injections of ragweed pollen extract are described. Of the 78 patients, 22 received a high final dose (above 1,000 protein nitrogen units), and 56 received less than 1,000 protein nitrogen units as a final dose. The majority of patients in the first group remained free from symptoms during the season or had only mild symptoms, whereas 53 patients in the second group had severe or moderate symptoms. It is concluded that high doses of antigen are necessary for the success of this method of treatment. [It is difficult to accept this conclusion without knowing the reason why a high dosage was not achieved in the second group. If, as it would appear, marked reactions at the injection site and constitutional reactions prevented a high dosage being given, this would indicate that the patients were difficult to hyposensitize rather than that smaller doses were less effective. In order to prove the author's contention, small and large hyposensitizing doses should have been given to 2 equal and unselected groups of patients.] *H. Herxheimer*

440. **Oral Cortisone in the Treatment of Hay Fever**
I. W. SCHILLER and F. C. LOWELL. *Journal of Allergy* [*J. Allergy*] **24**, 297–301, July, 1953. 9 refs.

A series of 51 patients with hay-fever (caused in most cases by ragweed and in others by grass pollen) who had been unsuccessfully treated by other methods received 100 mg. of cortisone daily by mouth in divided doses for 4 days. In 42 instances complete or satisfactory relief was obtained, mostly on the 1st or 2nd day of treatment. Relapse occurred between the 1st and 7th days after stopping the treatment in 20 cases. In the remainder the symptoms did not return although the pollen season was not over. *H. Herxheimer*

441. **A Clinical and Pathological Study of Fatal Cases of Status Asthmaticus**
J. C. HOUSTON, S. DE NAVASQUEZ, and J. R. TROUNCE. *Thorax* [*Thorax*] **8**, 207–213, Sept., 1953. 6 figs., 12 refs.

This paper is based on the findings at necropsy in 9 asthmatic patients who died at Guy's Hospital, London, in status asthmaticus but in whom there were no complications such as respiratory infection or pulmonary heart disease; all had developed their asthma in adult life (5 of them were over 40) and by chance 8 of the 9 were women. Possible aetiological factors included allergy in 4 cases, but unspecified psychological factors were considered to be equally important in 6 cases, and the majority had had severe asthma for many months before death.

Eosinophilia was a common finding. Death was sudden in all but 2 cases; only 2 of the patients had been given morphine in their final illness. Histological examination of the lungs after staining for collagen and elastic tissue, mucus and mucopolysacharides, and reticulin was carried out in 7 cases. The lumen of the smaller bronchi was found to be obstructed by mucus and by spirals of detached ciliated epithelium mixed with eosinophil leucocytes. This detachment of the superficial epithelium may follow crenation due to bronchial constriction and is considered to be a characteristic and most important finding, as the loss of ciliary activity must be an important cause of the accumulation of mucus and is probably the mechanism which proves fatal. The basement membrane was also thickened, there was only slight squamous metaplasia, and the mucous glands appeared to be normal. Emphysema was widespread, with marked thinning of the alveoli.

Several good photomicrographs showing the bronchial changes are reproduced. *K. Gurling*

442. **Fatal Bronchial Asthma. A Series of Fifteen Cases with a Review of the Literature**
B. V. EARLE. *Thorax* [*Thorax*] **8**, 195–206, Sept., 1953. 2 figs., bibliography.

The author presents a tabulated summary of the 160 fatal cases associated with bronchial asthma reported in the literature since 1922, and adds details of a further 15 cases seen at various hospitals in London and the provinces. From his analysis of the earlier reports he concludes that fatal asthma is not so uncommon as has been thought. Pathological findings which were common to the majority of the published cases included gross emphysema, plugging of bronchi with mucus, hypertrophy of bronchial walls with eosinophilic infiltra-

tion, and over-activity of the bronchial mucous glands. Asthma was the only or chief cause of death in 90 of the 160 cases. More than half the deaths occurred in patients aged between 40 and 60, and very few were in young adults. Complicating factors included bronchopneumonia, right ventricular hypertrophy, persistent thymus, and pneumothorax.

Of the 15 fresh cases presented, 9 were uncomplicated and 4 complicated with emphysema only; among the complicated cases were 2 with bronchitis and one each with bronchopneumonia and pulmonary infarct. The immediate cause of death is thought to be asphyxia due to bronchial plugging, bronchial spasm playing only a minor role, but aspirin, morphine, and adrenaline are drugs which may hasten death, and psychological factors may also play a part. Heart failure is not a common finding in uncomplicated asthma, but 3 of the 15 new cases were found at necropsy to have right ventricular hypertrophy. On the whole, prognosis is good during an attack of status asthmaticus, death in a young adult being very rare. Pulmonary infection is an important complication, tending to prolong the asthmatic attack and being difficult to diagnose. Resistance to pulmonary infection may be lowered by the prolonged use of adrenaline inhalers. *K. Gurling*

443. **Timed Vital Capacity in Bronchial Asthma**
M. J. DULFANO, J. A. HERSCHFUS, and M. S. SEGAL. *Journal of Allergy* [*J. Allergy*] **24**, 309–315, July, 1953. 3 figs., 8 refs.

In 36 cases of chronic bronchial asthma the vital capacity was recorded spirographically. In addition, the amount of air exhaled during the first second of the vital-capacity test was determined by means of an electric timing device, and the ratio between this volume and the total vital capacity calculated. In patients who were temporarily free from attacks this ratio was below that found in normal subjects, and it did not improve when a bronchodilator drug was administered. In patients observed during a spontaneous exacerbation of their chronic asthma the ratio was also smaller than normal and improved in only a few cases after the use of a bronchodilator drug, although in almost all cases the volume of air exhaled during the first second increased concomitantly with the vital capacity.

When asthma was induced in such patients by means of histamine or methacholine the ratio did not change, although the vital capacity was greatly reduced, nor was there any change in the ratio when the patient was protected against the effect of histamine or methacholine by an antispasmodic drug. It is concluded that the vital capacity itself is the more reliable guide to pulmonary function. *H. Herxheimer*

444. **Remission of Intractable Allergic Symptoms by Acute Intercurrent Infections**
J. H. FRIES and S. BORNE. *Annals of Internal Medicine* [*Ann. intern. Med.*] **38**, 928–934, May, 1953. 32 refs.

The authors report the beneficial effect of intercurrent infection on 16 patients treated for chronic severe allergic affections, including asthma, atopic dermatitis, and allergic rhinitis, at the Lutheran Hospital, Brooklyn, New York. The infective processes responsible for remission of symptoms were: measles, 11; pneumonia, 2; scarlet fever, 1; and upper respiratory tract infection with sore throat, 2 cases. Periods of remission varied from one week to one year. In addition, there was one case of coeliac syndrome, supposedly allergic in origin, which was regarded as "cured" after 5 years. In the majority of cases the remission was of several weeks' duration. The "anergic" phase usually began at the height of the febrile period.

The authors consider that the sustained pyrexia occurring during such infections is responsible for the beneficial effect on the allergic symptoms observed in their cases. They discuss the possibility that disturbance of the heat-regulating centres may lead to a release of ACTH, and point out that the inhibition of allergic response does not constantly follow such febrile reactions. *R. S. Bruce Pearson*

445. **Allergic Parotitis**
B. SWINNY. *Annals of Allergy* [*Ann. Allergy*] **11**, 473–474, July–Aug., 1953. 10 refs.

The case is described of a woman of 31 who had suffered for 9 years from an intermittent swelling of one or both parotid glands. She also had perennial hay-fever. Expression of the mucus blocking the left parotid duct produced a jelly-like cast, the leucocyte content of which was purely eosinophilic, and the nasal smear contained 20% eosinophils. The skin reacted strongly to many inhalants and foodstuffs. Consequently an elimination diet was tried, and it was found that omission of wheat completely cured the parotitis, while attacks were reported on three different occasions when wheat was eaten. Later the patient became tolerant of wheat in small amounts.

The author considers that allergic parotitis is a very rare condition; he has been able to discover only 25 previous cases which have been reported in the literature. *H. Herxheimer*

446. **Locust Sensitivity**
A. W. FRANKLAND. *Annals of Allergy* [*Ann. Allergy*] **11**, 445–453, July–Aug., 1953. 11 refs.

Allergic rhinitis, asthma, and irritation of the skin were found by the author, working at St. Mary's Hospital, London, to occur in laboratory workers who were in close contact with locusts (*Locusta migratoria* and *Schistocera gregaria*) at two anti-locust research institutions in Great Britain. Out of 34 such workers, 4 were severely affected, but in 14 others the only manifestation was a positive skin reaction; in 6 of these there was also a positive reaction to grass pollen. Four out of 7 patients with positive skin reactions to locusts had a positive reaction also to cockroaches, and it is suggested that cross antigenicity between the two allergens of these entomologically related insects may exist. In one case a preparation of locust faeces was successfully used for hyposensitization. *H. Herxheimer*

See also Pathology, Abstracts 344, 346, and 348.

Nutrition and Metabolism

447. **Time Factors in the Utilization of a Mixture of Amino Acids (Protein Hydrolysate) and Dextrose Given Intravenously**
R. ELMAN. *Journal of Clinical Nutrition* [*J. clin. Nutr.*] **1**, 287–294, May–June, 1953. 1 fig., 18 refs.

It has been known since 1937 that the efficient utilization of protein and the achievement of a nitrogen balance require the synchronous administration of carbohydrate and fat: if the carbohydrate is given separately the protein is less efficiently used and nitrogen loss occurs. Similarly, amino-acids are most efficiently used when they are given simultaneously. The literature on these phenomena is reviewed.

In the present study, carried out on 4 surgical patients at Barnes Hospital (Washington University School of Medicine), St. Louis, Missouri, amino-acids, in the form of protein hydrolysate, were administered intravenously before, after, or simultaneously with the administration of a 5% or 10% solution of glucose. The effects of various time relations on the nitrogen balance were observed. A positive nitrogen balance was achieved if the glucose and amino-acids were administered together, but the balance became negative if the same total amounts of amino-acids and glucose were given at separate times several hours apart. Also, better nitrogen retention was obtained with a slow, long infusion than with a short, quick one. There are thus two time-factors concerned—the rate of infusion of each nutrient, and the time of its administration in relation to the others.

C. L. Cope

MALNUTRITION

448. **Preliminary Report of an Investigation into the Effects of a Diet Free from Animal Protein.** (Voorlopige mededelingen omtrent een onderzoek naar het resultaat van voeding zonder dierlijke eiwitten)
W. F. DONATH, I. A. FISCHER, H. C. VAN DER MEULEN-VAN EYSBERGEN, and J. F. DE WIJN. *Nederlandsch tijdschrift voor geneeskunde* [*Ned. T. Geneesk.*] **97**, 2118–2122, Aug. 15, 1953.

In an attempt to elucidate further the question of the requirement of the human body for animal protein, the authors carried out clinical, biochemical, and metabolic investigations at the Netherlands Institute for Preventive Medicine, Leiden, on 60 individuals who, for various reasons and for various periods, had been taking a strictly vegetarian diet, the findings being compared with those of similar investigations on 52 control subjects who took a standard diet containing animal protein.

In comparison with the standard, the vegetarian diet was deficient in calories, total protein, carbohydrate, and calcium, and to some extent in vitamin D and inorganic phosphorus. These deficiencies were not generally reflected in the blood chemistry, but with prolonged vegetarianism (more than 2 years) their effect tended to become evident. The serum total protein level was not generally low in the vegetarians, but the albumin : globulin ratio was below normal. The blood cholesterol level tended to diminish progressively during the period of the diet.

In 8 cases the subject showed clinical signs of deficiencies, such as angular stomatis, lingual atrophy, and paraesthesiae (3), paradentosis, pyrrhoea, and recession of the gums (4), and diminished capillary resistance (1). Prolonged vegetarianism was associated with macrocytosis and slight anaemia which, with carotinaemia and low serum phosphorus and high serum alkaline-phosphatase values, are regarded as indicating early liver insufficiency. The preliminary conclusion is that vegetarianism is not without danger and that such a diet should be supervised medically. *R. Crawford*

449. **Amino-aciduria in Rachitic Children**
J. H. P. JONXIS and T. H. J. HUISMAN. *Lancet* [*Lancet*] **2**, 428–431, Aug. 29, 1953. 1 fig., 12 refs.

Having previously found that in rachitic children the urine contains unusually large quantities of amino-acids the authors, at the University Hospital, Groningen, carried out partition chromatography of the urine of 2 normal children and 3 with rickets (one with resistant rickets) before and after the administration of vitamin D_3.

They found that the excessive excretion of amino-acids was predominantly due to lysine, histidine, glycine+alanine, glutamic acid, and threonine+serine (the paired amino-acids were not satisfactorily separated), and that treatment with vitamin D_3 reduced the output, though not always to normal.

[It is interesting to note that the amino-acids found to be present in excess on partition are, by and large, those present in normal urine in the greatest amounts.]

G. A. Smart

450. **Hyperpiesis in Cardiovascular Beri-beri**
J. H. WALTERS. *Quarterly Journal of Medicine* [*Quart. J. Med.*] **22**, 195–214, April, 1953. 18 figs., 15 refs.

During the summer of 1951, 12 cases of severe acute cardiovascular beriberi, 11 of them in pearl-divers or their mates, came under observation at the State and American Mission Hospitals at Kuwait in the Persian Gulf; 9 of these cases are described. The clinical features were: acute onset, gross anasarca, myocardial damage, arterial hypertension which increased on treatment with thiamine, tachycardia, tenderness of the calves, and absence of signs (or minimal evidence) of peripheral neuritis. The diet of the divers consisted of polished rice and fresh fish, which were cooked in oil, and dates. In the absence of similar outbreaks in previous

years, the beriberi in these cases is attributed to the contamination of the rice with a fungus, which may have caused destruction of thiamine, and to the lack of meat and cheese. [The possible presence in the fish, even though cooked in oil, of thiaminase is not mentioned.] In 3 cases signs of scurvy were also present.

The cause of the oedema was not discovered; there was no reduction in serum protein level or evidence of acute or subacute nephritis, and it was not necessarily associated with cardiac failure. The initial hypertension, which rose on treatment with thiamine, may have been due to renal anoxia from increased tension within the renal capsule as a result of the oedema; then if treatment with thiamine caused an acute arteriolar constriction before the oedema had dispersed, the anoxia would be enhanced.

Severe myocardial damage occurred in some patients, and improvement did not always accompany treatment with thiamine. The electrocardiographic changes are described in detail. *H. M. Sinclair*

451. **The Anaemia of Adult Scurvy**

B. BRONTE-STEWART. *Quarterly Journal of Medicine* [*Quart. J. Med.*] **22**, 309–329, July, 1953. 6 figs., bibliography.

At Groote Schuur Hospital, Cape Town, 32 adults with clinically obvious (and in most cases severe) scurvy were studied during the period 1946 to 1950. All the patients were males—with one exception Bantus—and the average age was 36½ years. Coexisting deficiency or other diseases were very rare. A detailed study of the blood, bone marrow, and gastric secretion was carried out on 13 consecutive patients; these patients were kept on their customary native diet, consisting mainly of maize and containing 60 g. of protein, 20 g. of fat, 356 g. of carbohydrate, 22 mg. of iron, 1·2 mg. of aneurin, 0·65 mg. of riboflavin, and 15 mg. of nicotinic acid, providing altogether about 1,850 Calories; the ascorbic acid content was practically *nil*. They were first observed for control periods ranging from 1 to 30 days before ascorbic acid was given. During this time some of them were given vitamin B_{12}, folic acid, intravenous iron, or parenteral vitamin-B complex over a sufficiently long period for any haematological response to be seen. The other patients were observed mainly to determine the incidence and severity of the anaemia in adult scurvy and were given the full hospital mixed diet and synthetic ascorbic acid from the beginning.

In 10 of the 13 consecutive cases a rapid, complete haematological response followed the daily intravenous administration of 1,000 mg. of ascorbic acid while the patients were kept on the diet on which the scurvy with anaemia had developed. This response was elicited without the addition of proteins, amino-acids, iron, or other vitamins, whether the diet was deficient in these factors or not. It was found that intravenous iron, vitamin B_{12}, and folic acid had no influence at all on the blood picture or on the bone marrow, but all patients immediately responded to the addition of synthetic ascorbic acid. The anaemia was mainly normocytic and normochromic, but occasionally macrocytic in the more severe and prolonged cases. This macrocytosis was accompanied in one case in the present series with histamine-fast achlorhydria, and is occasionally found in association with leucopenia and myeloblastic bone marrow; these findings have sometimes led in the past to the erroneous diagnosis of pernicious anaemia.

Recent published studies on the relationship between folic acid and ascorbic acid in the metabolism of certain amino-acids and the reversion of the megaloblastic bone marrow of scorbutic monkeys to the normoblastic state after administration of folic or folinic acid have further focused attention on this problem. In the present series scorbutic anaemia in human adults completely failed, however, to react to the administration of folic acid or vitamin B_{12} in 3 cases studied. The bone marrow, often hypercellular, showed decreased mitosis; pepsin activity was normal. In a study of capillary fragility in these cases the formation of a haematoma was observed, but there appeared to be no correlation between the severity of the anaemia, the plasma iron level, and the extent of haematoma formation. An increase in the formation of haematomata by a positive-pressure cuff did not affect the anaemic state, but raised the faecal excretion of urobilinogen. While the plasma iron level, total iron-binding capacity, and faecal urobilinogen excretion were of no assistance in determining the mechanism of the anaemia, the haematomata appeared to be responsible for the low levels of plasma iron and iron-binding capacity which were present.

[This important, controversial paper ought to be read in the original by those interested in the possible participation of ascorbic acid in erythropoiesis. It helps to clarify, within the limits of the experiment, the "monistic" explanation of scorbutic anaemia.] *Z. A. Leitner*

METABOLIC DISORDERS

452. **Familial Idiopathic Methaemoglobinaemia Associated with Mental Deficiency and Neurological Abnormalities**

C. WORSTER-DROUGHT, J. C. WHITE, and F. SARGENT. *British Medical Journal* [*Brit. med. J.*] **2**, 114–118, July 18, 1953. 4 figs., 31 refs.

Idiopathic methaemoglobinaemia is a rare condition, and in this paper from the West End Hospital for Nervous Diseases and the Postgraduate Medical School, London, 3 cases occurring in one family are described. All 3 children were mentally defective and each had strabismus and some loss of deep limb reflexes. It is pointed out that congenital methaemoglobinaemia is not generally associated with mental defect or neurological abnormalities. In each case the cyanosis was controlled by administration of methylene blue in tablet form for 2 consecutive days in each week. In one patient methylene blue was demonstrably more effective than ascorbic acid, and intermittent dosage over a 2½-year period did not lead to any toxic effects. The patients had some polycythaemia, and their physical activity was not impaired. *D. A. K. Black*

453. **Weight Loss in the Obese. A Preliminary Communication**
A. KEKWICK and G. L. S. PAWAN. *Archives of the Middlesex Hospital* [*Arch. Middx Hosp.*] **3**, 139–149, July, 1953. 7 figs., 7 refs.

In this study the weight loss in obese patients was observed when they were given: (1) diets of varying caloric value, but with an approximately constant carbohydrate:protein:fat ratio; and (2) a series of three diets in which the daily caloric value was kept constant at 1,000 Calories and which contained 90% of protein, fat, and carbohydrate respectively. A fairly high salt and water intake was maintained in all cases. On the first series of diets the patient's weight was maintained while caloric values were 1,500 Cal. or more, but fell at lower caloric values; it was notable, however, that the rate of weight loss on diets of 1,000 and 500 Cal. did not differ significantly. With the 1,000-Calorie diets of differing composition, weight loss was greatest on the high-fat diet, somewhat less on the high-protein diet, while on the high-carbohydrate diet weight was maintained during the week of study.

Serial estimations of extracellular and total body water in patients who lost weight indicated that body-fluid loss did not completely account for the change in weight. There was nitrogen retention on the high-protein 1,000-Calorie diet, and on both the other 1,000-Calorie diets there was nitrogen equilibrium, indicating that loss of protein played no part in the loss of weight; this was supported by the absence of any increase in creatinine excretion. It was noted that the obese subjects did not develop ketosis on the high-fat diet, although one normal subject did so. In the obese patients the protein-sparing action of carbohydrate was no greater than that of fat. *D. A. K. Black*

454. **On Psychogenic Obesity in Children. IV.** [In English]
K. TOLSTRUP. *Acta paediatrica* [*Acta paediat. (Uppsala)*] **42**, 289–304, July, 1953.

The author presents the final instalment of the account of his studies on 40 obese children. He concludes that in 7 of his cases there was definite evidence of psychogenesis, in 11 psychogenesis was probable but not proven, while in 22 of the children there was no evidence that psychological factors were important in the aetiology of the obesity. The author stresses the importance of considering constitutional factors in connexion with the aetiology of obesity in children, and clearly demonstrates the lack of homogeneity in his group of cases when considered from an aetiological point of view.

A. C. Frazer

455. **The Effect of Corticotrophin in Idiopathic Steatorrhoea**
W. T. COOKE. *Lancet* [*Lancet*] **2**, 425–428, Aug. 29, 1953. 5 figs., 14 refs.

The effect of administration of ACTH (corticotrophin) on fat absorption and other defects of metabolism in 6 patients with idiopathic steatorrhoea was investigated at the United Birmingham Hospitals. ACTH was given by intramuscular or intravenous injection to a total dose of between 350 and 1,150 mg. The findings were similar to those reported by other workers, namely, a general increase in well-being in all the patients, a decrease in the water content of the faeces, a reduction in the excretion of fat, a positive nitrogen balance, and a normal prothrombin time during the ACTH therapy.

G. A. Smart

456. **Studies in Gout, with Particular Reference to the Value of Sodium Salicylate in Treatment**
F. G. W. MARSON. *Quarterly Journal of Medicine* [*Quart. J. Med.*] **22**, 331–346, July, 1953. 6 figs., 33 refs.

The author reviews the literature relating to the importance of urate deposition in chronic gout and of the reduction of the serum uric acid level in its treatment, and discusses the two available approaches to the therapeutic problem—by restriction of diet, and by the reduction of tubular reabsorption of urates in the kidneys by means of certain drugs, with particular reference to sodium salicylate.

He then describes the results of investigations carried out at the General Hospital, Birmingham, on 32 patients with chronic gout which had persisted for at least 3 months and was unrelieved by colchicine therapy. The effect of diet on the serum uric acid level was studied in 8 male patients who received alternately low- and high-purine diets, each for a period of 7 to 11 days. In 7 of the 8 patients the change from a low- to a high-purine diet was accompanied by a rise in the serum uric acid level, but the change was slight in degree and insufficient, in the author's opinion, for a low-purine diet to be of therapeutic value.

Continuous sodium salicylate therapy in a daily dosage of 60 to 140 grains (4 to 9 g.) was then attempted in 29 cases and was maintained in 14 of them for more than a year. In only one case did it prove impossible to reduce the serum uric acid level to within normal limits, and this patient was the only one with severe renal impairment. Intermittent treatment (for 3 consecutive days in each week) failed to maintain the reduction. All the patients experienced marked subjective improvement while receiving salicylates. In a few cases improvement was delayed for several weeks, but once started it was progressive. Reduction in the size of tophi took place, and in 2 instances tophi disappeared completely. Marked radiological improvement was observed in 4 cases. The maintenance of the serum uric acid content at a normal level did not necessarily prevent the occurrence of acute gouty attacks, for which colchicine was prescribed and usually afforded relief. Symptoms of salicylism usually appeared on starting treatment, but in most cases good tolerance developed after the first month. No haemorrhagic manifestations were observed, vitamin K being given when the plasma prothrombin concentration, which was estimated at frequent intervals, fell below 25% of normal.

The author claims to have shown very conclusively that continuous administration of sodium salicylate, in the absence of nephritis, can lower the serum uric acid level in chronic gout and thus ameliorate the symptoms and reduce the disability. *R. E. Tunbridge*

Gastroenterology

457. **Fulminating Gastroenterocolitis Caused by Staphylococci; its Apparent Connection with Antibiotic Medication**

K. Terplan, J. R. Paine, J. Sheffer, R. Egan, and H. Lansky. *Gastroenterology* [*Gastroenterology*] **24**, 476–509, Aug., 1953. 6 figs., 12 refs.

At the Buffalo General Hospital acute inflammation of the gastro-intestinal tract developed in 8 patients after various major surgical operations, such as hysterectomy, oophorectomy, gastro-enterostomy, and repair of a diaphragmatic hernia. Nausea and vomiting occurred in the immediate postoperative period, profuse watery diarrhoea and severe shock supervened, and the patient died 3 to 11 days after the operation. Necropsy revealed a pseudomembranous exudate on the mucous coat of the stomach and intestine. For the most part the inflammatory reaction was restricted to the mucosa and submucosa. Many staphylococci were found in the exudate, especially in the small intestine. Compact masses of these organisms were observed in the membranes lying in the lumen of the intestine. The membranes consisted of necrotic surface cells, fibrin, and leucocytes. Colonies of coagulase-positive haemolytic staphylococci were recovered not only from the intestinal tract (4 cases), but also from the lungs (2 cases). Degenerative changes were observed in the kidneys and adrenal glands. In most cases examination of the lungs revealed oedema and atelectasis. Apparently the staphylococci had produced a toxic condition, for no evidence of septicaemia was detected.

This severe inflammatory condition is attributed by the authors to the effect of antibiotic therapy upon the bacteria of the intestinal tract, the normal bacteria being replaced by pathogenic strains of *Staphylococcus aureus*. The antibiotics used in the present series of cases included oxytetracycline, aureomycin, chloramphenicol, and "syncrobin", a combination of penicillin and streptomycin. It is worthy of note that the staphylococci recovered from the lungs and intestines were sensitive to erythromycin, but not to the antibiotics used in treatment.

A. Garland

458. **Cytodiagnosis of Cancer of the Oesophagus.** (Le cytodiagnostic du cancer de l'œsophage)

J. Calvet, P. Marquès, C. Birague, H. Planel, and C. Azais. *Bulletin de l'Association française pour l'étude du cancer* [*Bull. Ass. franç. Cancer*] **40**, 39–44, 1953. 4 figs., 14 refs.

The authors describe a method of obtaining and examining smear preparations from the oesophageal mucous membrane in cases of suspected carcinoma of the oesophagus. The lesion is gently touched with a dry cotton-wool swab during oesophagoscopy, and imprint preparations then made without friction on slides. Alternatively, fluid may be aspirated through the oesophagoscope and centrifuged, the resulting deposit being spread on slides. The preparations are fixed, while wet, in a mixture of equal parts of 95% alcohol and ether and stained with haematoxylin and eosin. Thorough dehydration and clearing in carbolxylol are essential. As a rule, tumour cells are easily distinguished from normal epithelial cells and leucocytes.

A series of 21 cases of cancer of the oesophagus is reported in which both oesophageal smears and biopsy specimens were examined. In 9 cases both the methods gave positive results, and in 6 both gave negative results. In 5 cases the biopsy gave a positive result and the smear a negative one, while in one case the smear gave a positive result and a first biopsy a negative result; examination of a second biopsy specimen, however, confirmed the result of the smear. The method is recommended as an auxiliary to others, particularly when biopsy is difficult and radiography gives little information.

M. H. Salaman

STOMACH AND DUODENUM

459. **Effect of Large Doses of Histamine on Gastric Secretion of HCl. An Augmented Histamine Test**

A. W. Kay. *British Medical Journal* [*Brit. med. J.*] **2**, 77–80, July 11, 1953. 7 figs., 5 refs.

At the Western Infirmary, Glasgow, the author has studied the effects of augmented doses of histamine on the gastric secretion of hydrochloric acid in normal subjects and in patients with duodenal ulcer. In the histamine test of gastric secretion as usually employed the dose of histamine has been determined arbitrarily as being generally sufficient to provoke an acid response without being liable to cause untoward symptoms, and is thus a compromise which fails to take account of individual variations and susceptibility. This defect can be overcome by utilizing synthetic antihistaminics, which, as shown by Halpern (*Arch. int. Pharmacodyn.*, 1948, **74**, 314), antagonize all histamine effects save that on gastric secretion. In this way it is possible to give a maximum stimulus to the parietal cells. In the present investigation histamine was given subcutaneously, as histamine acid phosphate in multiples of the usual "body-weight" dose of 0·1 mg. per 10 kg. body weight, and mepyramine hydrogen malleate ("anthisan") was chosen as the antihistamine. In preliminary experiments it was found that in order to protect the patient against the systemic effects of histamine each "body-weight" dose of histamine had to be covered by 1 ml. (25 mg.) of mepyramine given intramuscularly 30 minutes before giving the histamine injection.

Secretion tests were begun after 12 hours' fasting. The fasting juice was first aspirated, and the subsequent collection of gastric juice made by continuous aspiration by

an electric pump. The spontaneous secretion was withdrawn for a period of 45 minutes before giving mepyramine, aspiration being then continued until the histamine injection was made, and thereafter for 45 minutes. The titratable free hydrochloric acid in the juice secreted after the injection was estimated and its content of HCl expressed in milligrammes. With these standard conditions and by increasing the amount of histamine by one " body-weight " dose at successive tests it was established in 12 patients tested that the maximum output of HCl followed the giving of 4 " body-weight " doses of histamine. In all cases maximum output was reached in 10 to 15 minutes and persisted for the next 30 to 35 minutes. The best measure of output, therefore, is based on the secretion during the half-hour period from 15 to 45 minutes after administration of histamine. Secretion during this half-hour period was estimated in each of the 12 patients on two or more occasions on successive days. Comparison of results in each series of tests showed an error of about 5%. The maximum HCl output of the stomach appeared to fall when aspiration at 15-minute intervals was employed, this being attributable to the loss of a considerable volume of gastric juice through the pylorus. The augmented histamine test provides two separate results (expressed in milligrammes of HCl as stated), the first figure indicating the basal secretion and the second being an expression of the maximum parietal-cell activity provoked by histamine.

Altogether 148 patients were examined, comprising 25 normal subjects, 103 with duodenal ulcer, and 20 with gastric ulcer; the diagnosis in the last two groups was confirmed at operation in every case. The results showed that in the normal subjects the average basal output of HCl was 70 mg. and the average maximum output 422 mg. In patients with duodenal ulcer the basal output averaged 265 mg. and the maximum 837 mg., while in patients with gastric ulcer the means were 113 and 478 mg. respectively. The authors conclude that 4 " body-weight " doses of histamine provoke an output of HCl which is constant for each individual and which represents the maximum parietal-cell output of acid. They regard gastric secretion of HCl as of an " all-or-none " nature, that is, there is no secretion by a parietal cell until an effective stimulus is applied and then the cell secretes maximally. The routine use of test meals is therefore futile, although in selected cases it may be of value in determining the presence or absence of free HCl. The advantages of this augmented histamine test are that it imposes a uniform stimulus which exerts a full load on the acid-secreting cells, and its results are repeatable.

E. Forrai

460. **Initial Depression of Human Gastric Secretion by Insulin**

W. H. Olson and H. Necheles. *Gastroenterology* [*Gastroenterology*] **24**, 362–368, July, 1953. 3 figs., 17 refs.

The effect of intravenous administration of insulin on gastric secretion in 15 male patients with duodenal ulcer was studied at Michael Reese Hospital, Chicago. The night before the test a Levin tube was passed into the stomach, and the following morning two control samples of gastric juice were taken. After an intravenous injection of 25 units of insulin, samples of gastric juice were taken at 15-minute intervals for a period of two hours. Venous blood for determination of the blood sugar level was withdrawn shortly before the insulin injection and at 30, 60, and 90 minutes afterwards. Forty tests were carried out, and in 33 there was a significant decrease in the volume of acid secreted during the first 45 minutes, the volume being at least 25% below the average. Thirty minutes after the insulin injection, when the blood sugar level was at its lowest, gastric secretion increased, reaching a maximum at about one hour. It appears that the initial fall in the blood sugar level depresses acid secretion (by a mechanism the nature of which is not clear), the increased flow corresponding to the return of the blood sugar level to normal.

K. Gurling

461. **Stimulating Effect of Vagotomy on Gastric Secretion in Heidenhain Pouch Dogs**

S. O. Evans, J. M. Zubiran, J. D. McCarthy, H. Ragins, E. R. Woodward, and L. R. Dragstedt. *American Journal of Physiology* [*Amer. J. Physiol.*] **174**, 219–225, Aug., 1953. 5 figs., 5 refs.

The hypothesis that vagotomy enhances the gastric phase of secretion was examined at the University of Chicago. It was found that in a dog in which a Heidenhain (vagally denervated) gastric pouch had been constructed, dividing the remaining vagal fibres resulted in a marked increase in secretion from the pouch in response to meals, but that no such increase occurred when the pyloric antrum had previously been resected from the main stomach; in this case the secretion from the pouch was much reduced. Section of the vagal supply to the main stomach in a dog with a Pavlov pouch did not significantly alter the secretion from the pouch in response to meals. When the fundus and corpus of the main stomach were resected in a dog with a Heidenhain pouch, leaving only the pyloric antrum between the oesophagus and the duodenum, there was a very considerable increase in the secretion from the pouch after meals.

It is suggested that abolition of the cephalic phase by vagotomy or resection of the fundus of the main stomach reduces the gastric acidity, and so releases the pyloric antrum from the inhibitory effect of acidity upon it.

R. A. Gregory

462. **Effect of Alkalis on Fasting Human Stomach**

J. S. Staffurth. *Lancet* [*Lancet*] **2**, 227–229, Aug. 1, 1953. 13 refs.

The author gives an account of an investigation carried out at St. Erik's Hospital, Stockholm, into the effect of the ingestion of alkalis on gastric secretion.

Of the 16 patients studied, 11 had a duodenal ulcer, 2 a prepyloric ulcer, and 3 had pain due to other causes. These patients were given 8 g. of sodium bicarbonate or magnesium trisilicate, and the acid secretion was studied over the next 2½ hours. The administration of a non-absorbable dye (phenol red) at the same time made it

possible to calculate the effects of emptying on the concentration of acid. The particular point investigated was whether there was a rebound secretion (that is, a rise to a greater level of acidity than in the fasting stomach) after the alkali had left the stomach as shown by the disappearance of the dye. Within the period of observation there was no evidence of such secretion, although in the majority of cases the alkali had left the stomach between 1½ and 2 hours after its introduction. There was no difference between the emptying time after the administration of sodium bicarbonate and that after magnesium trisilicate had been given, but the latter was less efficient as a neutralizing agent, presumably owing to poor mixing.

Other work on rebound secretion is reviewed, and it is concluded that in the dose usually given there is no danger of soluble alkalis causing an increase in gastric secretion. *T. D. Kellock*

463. **Development of New Symptoms following Medical and Surgical Treatment for Duodenal Ulcer**
J. S. Browning and J. H. Houseworth. *Psychosomatic Medicine* [*Psychosom. Med.*] **15**, 328–336, July–Aug., 1953. 18 refs.

An investigation was carried out at Indiana University and Cold Spring Road Veterans Administration Hospital, Indianapolis, to determine whether new symptoms arise after medical or surgical treatment of duodenal ulcer. A group of 30 patients who had undergone gastrectomy for duodenal ulcer and a control group of 30 treated medically for the same condition underwent a follow-up examination, which included radiological examination. It was found that while symptoms had been abolished by operation in over half the patients in the first group there was an increase in psychosomatic and psychoneurotic symptoms. In the second group the frequency and severity of the symptoms were not much reduced by medical treatment, but no increase in other symptoms was observed. The results suggest that surgical removal of an ulcer without resolution of associated emotional conflicts may lead to the development of new symptoms. *Desmond O'Neill*

464. **Pain in Chronic Gastric Ulcer. Basic Anatomy and Mechanism**
V. J. Kinsella. *Lancet* [*Lancet*] **2**, 353–361, Aug. 22, 1953. 13 figs., 35 refs.

To elucidate the mechanism of pain in chronic gastric ulcer the author, at St. Vincent's Hospital, Sydney, studied 650 microscopical sections of 22 ulcers removed at partial gastrectomy, the sections being stained to show the nerve fibres. Such fibres were scarce in the floor of the ulcers studied, and deeply embedded in the fibrotic layer; they were numerous, however, in the rolled edges. Those in the ulcer edge appeared similar to the "end-bulbs" of an amputation stump, there being histological evidence of nerve regeneration. Clinically, deep, punched-out ulcers with a floor of small area and rolled edges full of neural end-bulbs are very painful, whereas superficial shallow ulcers with a wide floor may be painless. This suggests that ulcer pain arises not from the floor of the ulcer but from its inflamed edges. If this is so, acid pepsin cannot be the primary cause of ulcer pain, although it may act indirectly by causing motor activity and vasodilatation in the ulcer edges.

The author repeats many of the arguments he has previously used (*The Mechanism of Abdominal Pain*, Sydney, 1948) in support of this hypothesis; these may be summarized as follows. (1) The layers of Askanazy in the floor of a peptic ulcer are insensitive to caustics; any nerve fibres in the floor of the ulcer lie in the deepest layer. (2) The fluctuations in ulcer pain are due to fluctuations in the degree of inflammation around the ulcer base. (3) The immediate relief of ulcer pain by vomiting or administration of food or alkalis is the result of altered blood flow through the ulcer base. (4) On clinical examination deep tenderness is localized to the ulcer area itself. (5) A close correlation is found at operation between the degree of inflammation around the ulcer and the severity of previous pain. (6) At operation under local analgesia the ulcer area is tender on palpation. *J. Naish*

465. **The Significance of Serum Iron in the Differential Diagnosis between Gastric Carcinoma and Peptic Ulcer.** [In English]
K. A. Fredrikson. *Acta medica Scandinavica* [*Acta med. scand.*] **146**, 259–267, Aug. 19, 1953. 10 figs., 10 refs.

The results of an investigation into serum iron values in patients suffering from gastric ulcer, duodenal ulcer, gastric carcinoma, and other malignant tumours are here reported from the University Medical Clinic, Turku, Finland. A photometric method was used to estimate the colour developed after potassium rhodanide and nitric acid were added to a protein-free filtrate of serum acidified with 6N hydrochloric acid. The mean serum iron value for 25 normal men was found to be $143{\cdot}3 \pm 35{\cdot}2$ μg. per 100 ml., and for 18 normal women $124{\cdot}2 \pm 32{\cdot}0$ μg. per 100 ml.

In the 14 cases of peptic ulcer and 24 of duodenal ulcer studied the serum iron values were within the normal range except after the occurrence of haemorrhage, when they were low. Low values ($64{\cdot}2 \pm 31{\cdot}6$ μg. per 100 ml.) were found in 13 patients with gastric carcinoma, whether or not occult blood was present in the faeces, and also in patients with other types of cancer ($75{\cdot}5 \pm 39{\cdot}8$ μg. per 100 ml.). The rise of the serum iron level 4 hours after an oral dose of 2·0 g. of ferrous lactate was also studied. In 11 healthy men the rise amounted to $49 \pm 56{\cdot}5$ μg. per 100 ml. Higher values were obtained in patients with peptic ulcer, namely, 109 ± 72 μg. per 100 ml. in 8 cases in which no haemorrhage had occurred and 249 ± 109 μg. in 8 cases with considerable post-haemorrhagic anaemia. In patients with cancer the rise in the serum iron level after oral administration of the ferrous salt was generally small, whether or not anaemia was present. In 7 cases of gastric carcinoma the rise was $28 \pm 23{\cdot}5$ μg. per 100 ml., and in 12 other types of cancer it amounted to $35{\cdot}5 \pm 22{\cdot}0$ μg.

The author concludes that an estimation of the serum iron content may be of value in the diagnosis of gastric

carcinoma, and that an iron tolerance test may help to distinguish between gastric ulcer and cancer. [But few clinicians would support these claims.]

D. G. Adamson

466. **The Choice of Operation in Perforated Ulcer of the Stomach and Duodenum.** (О тактике хирурга при прободной язве желудка и двенадцатиперстной кишки)
V. I. Struchkov. *Хирургия* [*Khirurgiya*] 3–6, No. 7, July, 1953.

The importance of early diagnosis and early admission to hospital in cases of perforated peptic ulcer is emphasized, and the surgeon is warned against the danger of being deceived by an apparent improvement in the condition of the patient during the first hours after admission into adopting expectant treatment. Operation should be performed as soon as the diagnosis is reasonably established, while in doubtful cases an early operation is much less dangerous than even a short delay. The author prefers local analgesia in such cases, although a high degree of skill on the part of the surgeon and extra time for the performance of the operation are required. The choice of operation is most important, and also most difficult. After an analysis of the long-term results of 1,200 operations for perforated ulcer carried out by several surgeons the author is in favour of simple suture of the perforation in patients under the age of 30 who have no previous history suggestive of peptic ulcer, or whose history is of a single acute attack ending in perforation. In a high proportion of such cases there is smooth recovery from the operation and complete freedom from dyspeptic symptoms for lengthy periods after it. In patients who give a long history of gastric trouble before the perforation, in whom the operation shows the presence of much scarring or signs of pyloric obstruction, and in all cases in which malignant change may be suspected, resection of the stomach is necessary.

P. T. Sander

467. **Resection of the Stomach as the Method of Choice in the Treatment of Perforated Ulcer.** (Резекция желудка как метод выбора при прободных язвах)
A. T. Lidskii and A. E. Norenberg-Charkviani. *Хирургия* [*Khirurgiya*] 7–11, No. 7, July, 1953.

The frequency of return of symptoms of peptic ulcer following operation for suture of a perforation makes necessary a revision of the question of the most suitable treatment for these cases. The high incidence of relapse among cases in which suture of the perforation was combined with gastro-enterostomy, a second operation showing scarring of the stoma and recurrence of ulceration, has led to the substitution of the more radical operation of gastrectomy whenever circumstances allow. Among the last 109 cases in which the authors performed primary gastrectomy for perforated ulcer there were only 2 operative deaths, one of them from the effect of the anaesthetic, whereas before 1952, when suture was the usual treatment, the mortality was between 14 and 18% before the introduction of penicillin, and 8·5% after it became available. It is pointed out, however, that other factors have contributed to a general reduction in operative mortality in recent years in Russia besides the antibiotics, such as a material improvement in the living conditions of the population, increasing interest in sports, better supplies of food, better conditions of labour, greater facilities for hospitalization, and increasing surgical skill. Clinically, recovery after resection is easier and more rapid than after suture, and complications are, as a rule, much less common. While the authors generally avoid gastrectomy in patients over 60, gastric haemorrhage is an imperative indication for resection regardless of age. Other important indications for resection are discussed, and it is recommended that simple suturing of a perforated ulcer be reserved for cases complicated by advanced cardio-vascular or pulmonary disease or advanced peritonitis, and for those in which it is technically impossible to perform resection.

P. T. Sander

468. **The Surgical Treatment of Perforated Ulcer of the Stomach. Results Obtained at the Sklifosovskii Institute in the Last 30 Years.** (Результаты хирургического лечения больных с прободными язвами желудка по наблюдениям Института имени Склифосовского за 30 лет)
B. S. Rozanov. *Хирургия* [*Khirurgiya*] 12–15, No. 7, July, 1953.

The surgeons of the Sklifosovskii Institute in Moscow were among the first in Russia to advocate resection of the stomach as a primary operation for perforated peptic ulcer. First performed in such a case in 1928, this operation is now a routine procedure if there are no clear contraindications to its performance. In cases where resection is considered to be too risky, suture of the perforation is carried out, gastro-enterostomy being added only on rare occasions when pyloric stenosis and distension of the stomach are present.

During the last 10 years resection for perforation has been performed on 961 patients, of whom 25 (2·6%) died after operation. At the same time 462 palliative operations were performed with a mortality of 12·6%. The administration of large doses of antibiotics by continuous absorption from the peritoneal cavity is a very useful complement to operation, but has no value in unoperated cases. In the author's opinion the results of resection could be further improved by the elimination of certain technical errors and the more careful selection of cases.

P. T. Sander

469. **The First Postoperative Days. A Study of Pre-ileus following Gastrectomy**
D. Ebrill and L. Naftalin. *Lancet* [*Lancet*] **2**, 411–417, Aug. 29, 1953. 9 figs., 8 refs.

In view of the occasional unpredictable failure of certain patients to make satisfactory progress after gastric operations, and in the hope of throwing some light on this problem, the authors carried out a biochemical study of serum electrolyte levels in 150 patients who had undergone subtotal gastrectomy at the County Hospital, Lincoln. The importance of the sodium–potassium

balance is stressed, with emphasis on the likelihood of overloading with sodium and depletion of potassium in the first 3 days after operation. From their study of the relation between ion balance and the proper recovery of intestinal activity, the authors conclude that three interrelated factors are concerned in the production of " pre-ileus ": (1) a sodium–potassium imbalance of 300 mEq.; (2) potassium depletion of about 125 to 150 mEq.; (3) this depletion must take place fairly rapidly, during the first 48 hours.

In discussing a suitable regimen for patients undergoing gastrectomy they suggest that preoperative gastric lavage and starvation should be avoided. An excessive intake of water in both pre- and post-operative periods is also undesirable, as it results in a loss of potassium in the urine. A mixture of potassium salts to be taken orally and a solution of potassium and sodium salts for postoperative replacement therapy are proposed and described. It is suggested that 6-hourly aspiration of the stomach is preferable to continuous aspiration through an indwelling tube. [It is difficult to understand, however, why the tube should be removed four times a day; nor is the term " pre-ileus " a good one, as it lacks definition.] *Guy Blackburn*

470. **The Causes of Post-prandial Attacks of Palpitation and Weakness after Gastric Operation**

W. H. SMITH, RUSSELL FRASER, K. STAYNES, and J. M. WILLCOX. *Quarterly Journal of Medicine* [*Quart. J. Med.*] **22**, 381–404, July, 1953. 6 figs., bibliography.

The postprandial attacks of palpitation and weakness which may develop after gastric operations are of two types: (1) early attacks which start during a meal or within half an hour of the beginning of a meal and which are usually described as dumping attacks; (2) late attacks occurring from 1½ to 3 hours after a meal and known to be due to hypoglycaemia. At the Postgraduate Medical School of London 17 patients who had typical attacks for at least 9 months after a gastric operation (gastrectomy in 14) were studied; of these, 7 had early (dumping) attacks, 8 had late (hypoglycaemic) attacks, and 2 had both. A comparison was made with a group of 9 patients who had undergone similar operations but who were free from such symptoms.

Radiological examination showed rapid emptying of the stomach in all the patients, but only in those who had dumping attacks was gastric emptying " precipitate "—that is, the stomach was empty 10 minutes after a standard barium meal and 60 minutes after a barium–glucose meal. In all the patients the oral glucose tolerance test revealed an unduly rapid initial rise in the blood sugar level and a slightly excessive hypoglycaemic rebound, but in the patients with dumping attacks the initial rise in the blood sugar level was " very rapid ", that is, the sum of the 15-, 30-, and 45-minute blood sugar values was over 600 mg. per 100 ml. The results of these tests did not differ as between the patients subject to hypoglycaemic attacks and the patients who were free from symptoms. The vasomotor symptoms of the dumping attacks present a syndrome suggesting the release of a vasoconstrictor substance like adrenaline; in 2 such cases similar effects were obtained by the gradual intravenous infusion of adrenaline, but attacks were not modified by administration of adrenergic-blocking drugs. Weakness and drowsiness in the patients with dumping attacks were associated with signs of hypopotassaemia and could be prevented by administration of potassium chloride. Hexamethonium bromide injected before meals considerably relieved the dumping attacks in 2 out of 4 patients, and also diminished the very rapid initial rise in the blood sugar level which, as described above, was otherwise obtained in response to the oral glucose tolerance test.

The patients who had hypoglycaemic attacks were distinguishable by the response to the intravenous insulin tolerance test, which showed abnormal persistence of hypoglycaemia, the sum of the 60-, 90-, and 120-minute blood sugar values being less than 180 mg. per 100 ml.; in all the other patients there was a similar, though much slighter, defect. An abnormally high level of insulin in the plasma was found in 3 patients after glucose had been given by mouth. The results of tests of anterior pituitary and adrenocortical function in 2 patients who had hypoglycaemic attacks were normal, indicating that there was no lack of insulin antagonists. The authors suggest that excessive insulin response, due to the rapid absorption of sugar, may be found in all patients subjected to gastrectomy, but that hypoglycaemic attacks are due to a greater degree of hyperinsulinism, which appears to be attributable to " nervous reactivity ". *Joseph Parness*

See also Pathology, Abstract 339.

LIVER AND GALL-BLADDER

471. **Needle Biopsy of the Liver. Clinical Evaluation of 323 Biopsies; Report of Two Cases of Accidental Biopsy of the Gallbladder**

R. D. GAMBLE and B. H. SULLIVAN. *Gastroenterology* [*Gastroenterology*] **24**, 394–404, July, 1953. 14 refs.

At the Brooke Army Hospital, Fort Sam Houston, Texas, during the period November, 1948, to July, 1952, 231 patients were subjected on 323 occasions to Vim–Silverman needle biopsy of the liver through an intercostal approach; there were no deaths, and no complications such as subcutaneous emphysema, local haematoma, or pneumothorax. In 2 cases, however, gall-bladder biopsy was performed accidentally, though with no serious consequences. Of a series of 50 consecutive cases studied in more detail, there was mild or moderate pain either during or after the examination in 31 cases, and severe pain in 6; in this series no tissue was obtained on 6 occasions and unsatisfactory specimens on 9—a failure rate of 30%.

The authors consider that 81% of the biopsies were of definite aid in establishing the clinical diagnosis, and that 48% of them significantly influenced either the treatment or the disposal of the patient. The biopsy findings appear to have been of most value [as is the experience of other workers] in cases of chronic hepatitis; in 2 cases

the patient was found to have acute hepatitis without jaundice and without symptoms of liver disease. A clinical diagnosis of portal cirrhosis was confirmed by liver biopsy in approximately two-thirds of the cases examined, and of chronic hepatitis in one-third. Some of the literature on liver biopsy, particularly with regard to morbidity and mortality, is reviewed, and 7 of the main contraindications to the procedure are listed. The authors conclude that this examination is probably the most useful single test in the assessment of liver disease.

Thomas Hunt

472. **Hepatic Coma. A Clinical, Laboratory and Pathological Study**

S. C. CARFAGNO, R. F. DEHORATIUS, C. M. THOMPSON, and H. P. SCHWARZ. *New England Journal of Medicine* [*New Engl. J. Med.*] **249**, 303–309, Aug. 20, 1953. 3 figs., 20 refs.

In this paper 11 cases in which clinical observation suggested advanced hepatic insufficiency and which were followed to necropsy are reported from the Philadelphia General Hospital. The authors consider that these cases satisfied the criteria for the diagnosis of hepatic coma, namely, the presence of lethargy or unconsciousness, fœtor hepaticus, jaundice, spider angiomata, hepatomegaly, and ascites. Extensive laboratory studies were carried out in all cases. A review of the results of routine blood and liver function tests serves to emphasize the lack of sensitivity of these tests for predicting or measuring hepatic coma. The maintenance of normal blood sugar or blood urea nitrogen levels in most of these cases does not detract from the significance of a reduced level in the individual case with advanced parenchymal failure. In all cases the post-mortem finding of advanced hepatic disease confirmed the clinical impression of coma from hepatic causes. The serum bilirubin level was elevated in all cases, markedly so in some, as would be expected with severe parenchymal degeneration or infiltration. The uniform presence of jaundice in cases of chronic liver disease which terminated fatally emphasizes the seriousness of this finding in patients with cirrhosis.

Cephalin–cholesterol flocculation was generally positive (24-hour reading), whereas that of thymol was usually negative until 18-hour flocculation was recorded. Serum alkaline-phosphatase levels were normal or low, except in one case with nodular metastases. This finding in the presence of hyperbilirubinaemia could best be explained on the hypothesis of impaired regenerative activity of cholangiolar cells. The estimation of serum lipid levels showed a decrease in those of cholesterol and cholesterol esters and of phospholipids; those of neutral fat and fatty acid showed no such consistent change. The serum pyruvic acid level was above the normal of 1 mg. per 100 ml., and that of lactic acid above the normal of 10 mg. per 100 ml.

The authors began their study on the assumption that one factor in hepatic coma which contributed to the altered physical state was a breakdown in intermediate carbohydrate metabolism, this failure of full utilization of carbohydrate probably occurring at the tricarboxylic cycle. The finding of elevated blood pyruvic acid, blood lactic acid, and, in one case, α-ketoglutaric acid levels seems to confirm this. The failure of enzyme systems within the fatty, fibrotic, or infiltrated liver would probably impair the phosphorylation of thiamine, which is necessary for complete utilization of pyruvic acid. In the authors' view there is much to support the proposition that the biochemical disturbance in thiamine deficiency is an inability of the cell to metabolize pyruvic acid. Lactic acid metabolism is affected by many of the same factors as that of pyruvic acid, among which are liver injury, nutritional deficiency, and anoxia. Liver injury leads to the accumulation of lactates because of failure to convert lactate into glycogen and of its subsequent storage. The possibility of ammonium intoxication and its resemblance to hepatic coma are discussed briefly. The post-mortem findings showed that most patients with terminal hepatic insufficiency had an increase in liver weight. There was no disagreement in the histological interpretation of the hepatic tissues examined microscopically.

E. Forrai

473. **Experimental Analysis of the Effects of Vagotomy on the Tone of the Biliary Tract.** (Analyse expérimentale des effets des opérations de vagotomie sur le tonus des voies biliaries)

P. MALLET-GUY, J. DESCOTES, A. AHUALLI, and A. VENTURINI. *Lyon chirurgical* [*Lyon chir.*] **48**, 685–703, Aug.–Sept., 1953. 10 figs., 25 refs.

Experiments on dogs were undertaken at the Lyons Faculty of Medicine in order to elucidate the effect of vagotomy on the biliary tract. The activity of the biliary tract was recorded radiographically after the injection of a specially-prepared " ultrafluid " iodized oil into the gall-bladder to display the gall-bladder and large ducts, and manometrically by the method used by one of the authors during operations on the biliary tract. Such records required only the insertion of a needle into the gall-bladder and could be obtained on several occasions from the same animal. The vagus nerves were sectioned in the neck or above or below the diaphragm in some cases, and in others only those branches running along the lesser curve of the stomach were sectioned. Division was always preceded by procaine infiltration to avoid any stimulation. *X*-ray and pressure records were made before, and again either immediately or 3 to 7 days after, nerve section. In some experiments both immediate and delayed observations were made.

The results are given of 67 valid experiments out of 96 attempted. Unilateral cervical vagotomy was carried out in 20 (10 left, 10 right), and vagotomy above or below the diaphragm in 30 (7 bilateral, 12 right, 11 left), while the nerves along the lesser curve were cut (" low bilateral vagotomy ") in 17 experiments. Records were made after vagotomy on 82 occasions. All the animals were eventually killed and the completeness of the vagotomy verified.

Although 23 of the 82 observations showed no definite change following vagotomy, in the majority the pressure was reduced and the cholangiogram showed changes indicating a diminution of tone. In some instances the medium left the ducts very rapidly [presumably because

of absence of tone in the sphincter of Oddi]. Pigment calculi sometimes formed and blocked the common duct as a result of stasis after vagotomy. Comparison of the effects of the various nerve sections performed showed that the biliary tract is innervated by both vagi, though mainly by the left, and is most effectively interrupted by section along the lesser curve. Cervical vagotomy was relatively ineffective.

It is concluded that in the treatment of syndromes associated with hypertonus of the sphincter of Oddi low vagotomy along the lesser curve is the operation of choice.

C. J. Longland

PANCREAS

474. Carcinoma of Body and Tail of Pancreas

C. STRANG and J. N. WALTON. *Annals of Internal Medicine* [*Ann. intern. Med.*] **39**, 15–37, July, 1953. 21 refs.

The clinical and pathological findings in 58 cases of carcinoma of the body and tail of the pancreas seen at the Royal Infirmary, Newcastle upon Tyne, during the 20-year period 1932–51 are here reported. An analysis of the hospital records showed that carcinoma in this situation occurred once in every 5,993 cases admitted, and that out of a total of 9,167 necropsies, carcinoma of the head or whole of the pancreas was found in 39 and of the body or tail in 21, an incidence at necropsy of 6·5 per 1,000 and 2·3 per 1,000 respectively. Symptoms had been present for an average of 4·5 months, and the commonest presenting symptom (41 cases) was epigastric abdominal pain, which was usually intermittent, and varied considerably in character and duration. Anorexia (37 cases) and loss of weight (51 cases) were common. Lassitude was often a marked feature and could lead to a false diagnosis of hysteria. An abdominal mass was palpable in 26 cases and was commonly due to metastatic deposits. In 18 cases there was tenderness on palpation in the epigastrium. Glycosuria was rare. Stools were examined in 2 cases and found to be abnormal and to contain excessive fat. Distortion of the gastro-intestinal tract was observed in 4 of the 20 cases in which radiological examination was carried out. The commonest site of the metastatic deposits was locally in the abdomen or the liver. As might be expected, the detailed symptomatology in each case depended essentially on the exact location and the extent of the primary growth and the secondary deposits.

A. C. Frazer

475. Pancreatic Cysts—Surgical Treatment Especially by the Use of Internal Drainage, with a Report on Six Cases

A. L. ZAOUSSIS. *Annals of Surgery* [*Ann. Surg.*] **138**, 13–23, July, 1953. 4 figs., bibliography.

The author reviews the results of internal drainage operations for pancreatic cysts in 6 personal cases treated at the Hellenic Red Cross Hospital, Athens, and in 98 cases collected from the literature up to March, 1952, a total of 104 cases.

In 50 patients in whom the cyst had been anastomosed to the back of the stomach (in 29 cases by the transgastric route) there were 2 immediate deaths, but in 45 of the 48 survivors the results were good. Although the fear has often been expressed that the gastric contents will pass freely into the cyst cavity after cystogastrostomy, such reflux was demonstrated radiologically in only one case in this series; in that case the repair was subsequently converted to a cystojejunostomy with good results. In 33 cases the cyst was drained into the jejunum, the anastomosis in 8 of these being made to a defunctioned Roux–Y loop, in 9 to an ordinary jejunal loop with entero-anastomosis, in 12 to a simple jejunal loop without anastomosis, and in 4 by an unspecified technique. In this group there were 2 deaths resulting from leakage and in 2 cases the cyst recurred, presumably owing to poor drainage and closure of the stoma. In the remaining 29 cases the immediate results were good, though in one case radiological examination demonstrated reflux of barium into the cyst from the jejunum.

Internal drainage into the gall-bladder, sometimes combined with ligation of the cystic duct, was employed in 11 cases. There was one immediate death from cerebral haemorrhage, and one late death from rupture of an imperfectly draining cyst 8 months after operation. In most of the other 9 cases the clinical results were mediocre and the author does not recommend this procedure, although theoretically it appears promising. Finally, in 10 cases the cyst was drained into the duodenum at the point adjacent to the head of the pancreas, a transduodenal technique being usually employed. The results were excellent in 8 cases.

From this survey the author concludes that internal drainage operations for pancreatic cysts are procedures of established value, and that the most useful and satisfactory techniques are cystojejunostomy, using a Roux–Y type of anastomosis, and cystogastrostomy.

J. C. Goligher

476. External Sphincterotomy for Pancreatitis

L. GILLETTE. *Annals of Surgery* [*Ann. Surg.*] **138**, 24–32, July, 1953. 8 figs., 26 refs.

In this paper from the Gouverneur Hospital, New York, the author describes a new method of dividing the thickened and fibrosed sphincter of Oddi which is often found in cases of chronic pancreatitis. The procedure is based on the principle of the Ramstedt and Heller operations for hypertrophic pyloric stenosis and cardiospasm respectively, and consists of an extramucosal myotomy of the sphincter muscle. Through a supraduodenal choledochotomy a probe is passed down the common bile duct and through the sphincter of Oddi into the duodenum. The latter is then mobilized by the Kocher manœuvre, exposing the head of the pancreas from behind. The lower end of the common duct is exposed and the muscle fibres of the sphincter of Oddi are carefully divided, partly by cutting and partly by divulsion with artery forceps, until the mucosa of the duodenum and common duct pouts freely. Special care is taken to leave no sphincter musculature in the angle between the duct and the duodenal wall. Finally the probe is removed and a T-tube inserted into the common duct.

Of 5 patients treated by this method so far, there was complete relief of symptoms in 4, but the result was poor in the 5th case, in which the division of the sphincter muscle was thought to have been incomplete.

[This would seem to be a much more difficult technique than that of transduodenal or endodochal sphincterotomy, and if the musculature is thoroughly divided it must surely be difficult occasionally to avoid perforation of the mucosa.] *J. C. Goligher*

INTESTINES

477. **The Treatment of Constipation with a New "Hydrasorbent" Material Derived from Kelp**
M. G. Mulinos and G. B. J. Glass. *Gastroenterology* [*Gastroenterology*] **24**, 385–393, July, 1953. 2 figs., 5 refs.

The authors report from the Flower and Fifth Avenue Hospitals (New York Medical College), New York, a method of treatment of constipation with a water-absorbing substance derived from kelp (dried sea-weed). The preparation used was a mixture of the calcium and sodium salts of alginic acid, which has the property of swelling in an alkaline medium but does not absorb water at all at a *p*H below 5, so that no change occurs in normal gastric juice. The absorption of water in conditions similar to those prevailing in the intestine was about six times greater than that of a typical gum-type laxative derived from plantago, and also greater than that of methylcellulose or psyllium seed. The alginate in the form of a powder was found to work better than in tablet form and was well tolerated by patients. It swelled to between 25 and 35 times its bulk in intestinal juice, and seemed to provoke increased rate of colonic emptying without irritation and with symptomatic relief of constipation. Of 30 patients treated with powdered alginate, in 20 the result was excellent, in 6 good, and only 4 were regarded as failures. *Thomas Hunt*

478. **Primary Resection of the Colon in Acute Ulcerative Colitis**
C. B. Ripstein. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **152**, 1093–1095, July 18, 1953. 5 figs., 3 refs.

The author has carried out total colectomy in 120 cases of ulcerative colitis, and in the present paper he describes the results of primary colectomy with ileostomy in 45 of these, which were of the acute fulminating type.

The operation was performed through a left rectus incision, the terminal ileum being brought out through a stab wound in the right iliac fossa. Before establishing the ileostomy frozen sections of the terminal ileum were examined histologically to make certain that the exteriorized bowel was free from disease. The divided rectosigmoid was also exteriorized, through a stab wound in the left iliac fossa, the residual stump of rectum and rectosigmoid being excised 3 to 6 months later.

All the patients were in a toxic state, with severe diarrhoea and a temperature of 103° to 105° F. (39·4° to 40·6° C.). In 6 cases massive haemorrhage was a complicating factor, in 8 perforation had occurred, while in 3 there was evidence of metastatic infection and in 2 carcinoma of the colon. There were 2 postoperative deaths (1 from septicaemia and endocarditis and 1 from peritonitis and intestinal obstruction).

In the author's opinion the indications for this procedure are: (1) failure of medical treatment to bring about a remission within 3 weeks (an arbitrary period, but based upon the author's experience that further delay is dangerous); (2) occurrence of perforation or signs and symptoms of impending perforation; (3) continued or repeated haemorrhage; (4) presence of septicaemia or metastatic infection. *C. Patrick Sames*

479. **Idiopathic Ulcerative Colitis Beginning after the Age of Fifty**
B. M. Banks and M. I. Klayman. *New England Journal of Medicine* [*New Engl. J. Med.*] **249**, 91–96, July 16, 1953. 17 refs.

Twenty cases of idiopathic colitis beginning after the age of 50 and followed from onset to the date of this survey are reported. This represents an incidence of 10% of all patients with this disease admitted to the Beth Israel Hospital [Boston] from 1941 to 1952 inclusive.

Among the factors implicated in precipitating the original or subsequent attacks were emotional stress, overdose of cathartics, administration of anticoagulants, use of cortisone and repeated catheterization for urinary retention. Early diagnosis in many cases was hindered by the deceptively mild symptomatology, the stoicism of the patient, his excellent nutritional status and the co-existence of more impressive organic disease. Sigmoidoscopy was the most valuable single diagnostic procedure.

Eleven patients in their first attack responded promptly and favourably to the usual medical measures, and 10 of these were living and well an average of five and six-tenths years later. Nine patients required major surgical procedures (5 on the first admission), with a relatively high mortality rate. In the patients who survived operation the symptoms of the original disease have not recurred.

Ulcerative colitis beginning after the age of 50 years is often as serious and fatal a disease as it is in the younger age groups. Although in our experience the prognosis in the older patient after recovery from one attack is relatively good, with the advent of the second attack it becomes much more guarded.—[Authors' summary.]

480. **The Clinical Diagnosis and Treatment of Colitis due to Protozoa.** (К клинике и лечению больных протозойными колитами)
Y. A. Il'inskii. *Клиническая Медицина* [*Klin. Med. (Mosk.)*] **31**, 63–68, June, 1953. 5 refs.

The clinical picture of the various types of protozoal colitis is varied and often difficult to recognize. In this article 39 cases are described—9 of pure amoebiasis, 3 of combined amoebic and bacillary dysentery, 5 of balantidiasis, 18 of lambliasis, and 4 of *Trichomonas* colitis.

The majority of the cases of amoebiasis were of the chronic recurrent type; in 2 there was an acute bacillary

dysentery superimposed on a chronic amoebic infection, while one patient had an amoebic abscess of the liver. In the 2 acute cases the haemoglobin levels were 12% and 20% respectively; in the chronic cases it varied from 56 to 70%. Mild leucocytosis was present in the acute cases, but leucopenia was the rule in the chronic stage and eosinophilia was found only in the stage of recovery. Sigmoidoscopy showed localized hyperaemia and ulceration in only one case; in the rest the mucous membrane was pale and opaque. The specific amoeba or its cysts were found in 10 of the 12 cases, but the clinical picture was clear in the remaining 2 and they responded to specific treatment with 1·5 ml. of a 2% solution of emetine hydrochloride given twice daily by intramuscular injection for 5 days, a second course being given after 7 days' rest. In the interval 0·25 g. of "yatren" was given thrice daily, while enemata of gramicidin (100 ml. of 0·08% solution) were given daily during the courses of emetine. In 3 cases aminarson [a Soviet preparation of aminarsol?] was given in doses of 0·25 g. 4 times a day for 7 days, alternating with a course of yatren of the same duration in the dosage described above. In 2 other cases viomycin was tried in doses of 1 g. for 2 days and 2 g. for 3 days, followed after 5 days' interval by 2 g. daily for 5 days. This was found extremely effective.

Colitis due to *Balantidium* infestation responded well to courses of aminarson, and also to viomycin. The best mode of treatment of *Lamblia* infestation was with acrichin (mepacrine) in doses of 0·1 g. 4 times daily for 5 to 6 days, repeated if necessary at intervals of 10 days. Viomycin was not so effective in this form of infestation. *Trichomonas* infestation yielded to aminarson in the same dosage as above, and in some cases to viomycin. This last the author regards as the best treatment for all types of protozoal colitis except lambliasis.

L. Firman-Edwards

481. **Congenital Megacolon. A Comparison of the Spastic and Hypertrophied Segments with Respect to Cholinesterase Activities and Sensitivities to Acetylcholine, DFP and the Barium Ion**

K. Kamijo, R. B. Hiatt, and G. B. Koelle. *Gastroenterology* [*Gastroenterology*] **24**, 173–185, June, 1953. 5 figs., 17 refs.

The authors, at Columbia University, New York, have carried out pharmacological investigations upon isolated strips of colon obtained from 5 patients with Hirschsprung's disease, using similar material from a patient with ulcerative colitis as a control. They found that in the cases of Hirschsprung's disease there was a higher threshold of response to acetylcholine, and a higher concentration of cholinesterase, in the distal, undilated segment than in the proximal dilated segment. The higher level of cholinesterase, in respect of the concentration of both specific and non-specific enzymes, was of the same order as that found in the control material from the case of ulcerative colitis. It is considered that the low level of cholinesterase activity in the hypertrophied segment was due to the failure of the enzymes to increase in proportion to the general increase in bulk of the structures constituting the wall of the colon. The higher threshold of response to acetylcholine in the spastic loop was probably due to the fact that the drug acted directly on the smooth muscle, whereas in the dilated loop it acted on the neural elements. The response of both segments to di-*iso*propylfluorophosphate and the barium ion was approximately equal.

Histological examination confirmed the absence of ganglion cells and the presence of an abnormally large number of medullated nerve fibres in the distal segment. The authors postulate that these medullated fibres are the post-ganglionic fibres of cells which are normally located in the myenteric plexus, but which in Hirschsprung's disease are located outside the wall of the gut. The fact that the barium ion acted equally on segments with and without ganglion cells indicates that its site of action is the muscle cell itself. The muscle of the specimen from the case of ulcerative colitis showed no regional variation in activity, pharmacological response, or cholinesterase content.

A. G. Parks

482. **Strangulation of Intestinal Herniae through Openings in the Mesentery, Omentum, and Broad Ligament of the Uterus.** (Ущемление кишок в отверстиях брыжейки, сальника и широкой связки матки (по данным лечебных учреждений Украины)

D. P. Chukhrienko. *Хирургия* [*Khirurgiya*] 47–54, No. 7, July, 1953. 5 figs.

Among 5,614 cases of intestinal obstruction, strangulation of a segment of bowel which had herniated through an aperture in the mesentery or broad ligament was found in 52 cases, or less than 1%. The origin of such mesenteric apertures is obscure and although many different hypotheses have been put forward, none of them adequately explains the involution and disappearance of the tissue of the mesentery. In a few cases the opening may result from injury to the abdomen or may have been made by the surgeon in the course of a previous abdominal operation. The precise diagnosis before operation is impossible, and in nearly all the cases here reported the operation was performed under the non-committal diagnosis of "unspecified intestinal obstruction".

Any section of the intestinal tract may be involved, as may a portion of omentum, a Meckel's diverticulum, or the appendix, but a loop of small intestine, sometimes with a portion of large intestine, is the most common; in certain cases in the present series the strangulation was accompanied by volvulus or by rupture of the mesentery, with haemorrhage from the mesenteric blood vessels. Similarly, the aperture may occur in any part of the mesentery—in one case it was situated in the mesentery of the appendix, in 5 cases hernia occurred through a hole in the mesentery of the transverse colon which was definitely of traumatic origin, in another 4 cases the aperture was in the mesentery of sigmoid colon, and in one the hernia was not through a hole but into a pocket in the mesentery. In one case the whole of the small intestine, with the exception of the duodenum, was found strangulated. In only one case was the aperture situated in the broad ligament of the uterus; no similar case was recorded among 313 cases recorded in the literature at the author's disposal.

P. T. Sander

Cardiovascular System

483. **The Surgical Treatment of Portal Hypertension.** (Хирургическое лечение портальной гипертензии) F. G. Uglov. *Вестник Хирургии* [*Vestn. Khir.*] **73**, 45–50, May–June, 1953.

The author describes a case of portal hypertension, in which the patient presented with symptoms of recurrent massive haematemesis, which was successfully treated by lateral portacaval anastomosis, the technique used being that previously described by Blakemore. It is claimed that this is the first successful operation of this type in Russia. *Z. W. Skomoroch*

484. **A Mechanical Heart–Lung for Use in Man**
D. G. Melrose. *British Medical Journal* [*Brit. med. J.*] **2**, 57–62, July 11, 1953. 9 figs., 36 refs.

An artificial heart–lung machine, devised to assist the circulation in coronary thrombosis, acute pulmonary oedema, congestive heart disease, and cardiac surgery, is described in this paper from the Postgraduate Medical School of London. The " heart " consists of two rotary pumps of a modified Henry–Jouvelet type, one withdrawing blood and feeding it to the " lungs ", the other receiving blood from the " lungs " and returning it. These input and output systems are automatically regulated to keep the volume of blood in the machine constant. The " lung " consists of a rotating cylinder of perspex, with internal annular plates over which the blood is spread and exposed to an atmosphere of oxygen as it passes by gravity through the cylinder. For efficient use this oxygenator requires charging with 0·5 to 2·0 litres of blood. A steady output of 2 litres of oxygenated blood is reported, with minimal haemolysis and no foaming. Under these conditions the oxygenator can supply 205 ml. of oxygen per minute. A method of sterilization is described. *W. J. H. Butterfield*

485. **Experimental Physiology of a Heart–Lung Machine in Parallel with Normal Circulation**
D. G. Melrose, J. W. Bassett, P. Beaconsfield, I. G. Graber, and R. Shackman. *British Medical Journal* [*Brit. med. J.*] **2**, 62–66, July 11, 1953. 8 figs., 7 refs.

A series of experiments were carried out at the Buckston Browne Research Farm, Kent, on 30 healthy dogs to determine the value of a heart–lung machine [see Abstract 484] in resuscitation and in the treatment of failing circulation. The animals were anaesthetized and, for a period of an hour, blood was taken from the inferior vena cava into the apparatus, oxygenated, and returned, usually to the femoral arteries. Although 4 dogs did not survive the procedure, death was not directly attributable to the apparatus. The remainder were fit until they were killed 3 months after the operation. The most marked effect of the procedure on the blood was to reduce both the platelet and leucocyte counts. The sodium, potassium, and chloride content of the plasma, the blood sugar level, and the blood urea level were unaffected. The plasma CO_2 combining power and *p*H of the blood revealed a tendency towards CO_2 deficit. In 7 out of 12 animals the cardiac output fell by an amount approximately equal to the rate of infusion from the machine. In other experiments, on 6 dogs, it was found that during the inspiration of pure nitrogen the oxygen saturation of the blood in the carotid artery did not fall below 50%, provided the oxygenated blood (given at the rate of 1 litre per minute) was returned to the thoracic aorta or the superior vena cava.
W. J. H. Butterfield

HEART FAILURE

486. **Cation Exchange Resin (Resodec) in the Treatment of Cardiac Oedema**
A. A. F. Peel and T. Semple. *British Heart Journal* [*Brit. Heart J.*] **15**, 350–356, July, 1953. 22 refs.

"Resodec", a balanced carboxylic cation-exchange resin in the ammonium–potassium form, was used at the Victoria Infirmary, Glasgow, 14 times in 10 patients with refractory or recurrent congestive cardiac failure. Except in 5 of the 14 courses the patients were given an ordinary ward diet, with the addition of 45 g. of the resin daily in divided doses. Definite weight reduction occurred during 9 of the courses, with disappearance of oedema in 4. Various side-effects were noted. Hyperchloraemia could be combated by salt restriction; conversely, the resin tended to restore serum chloride levels to normal in those patients who developed hypochloraemia on a low-salt diet. Both hypo- and hyperkalaemia occurred in a few cases, the latter associated with a rise in the blood urea level in those patients with defective renal function. One patient developed digitalis intoxication while taking the resin. The authors stress that strict biochemical control is essential during treatment, and emphasize that the present study was confined to patients who had previously proved refractory to treatment with digitalis and mercurial diuretics. Most of the patients complained that the resin left a lingering, sticky feeling on the lips, tongue, and palate, and many preferred dietary restriction to a free diet with the resin.
A. Paton

487. **Use of a New Oral Diuretic, " Diamox ", in Congestive Heart Failure**
H. Belsky. *New England Journal of Medicine* [*New Engl. J. Med.*] **249**, 140–143, July 23, 1953. 6 refs.

The use of a new oral diuretic, " diamox " (acetazoleamide or 2-acetylamino-1:3:4-thiadiazole-5-sulphonamide), in the treatment of 13 cases of congestive failure is described in this paper from the Mount Vernon

Hospital, New York. This substance, which is a specific inhibitor of carbonic anhydrase, promotes renal loss of bicarbonate, sodium, potassium, and water. A daily dose by mouth of 1 g. or more gave rise to paraesthesiae and numbness in the face and extremities and to drowsiness. These toxic effects became minimal when the daily dose was 0·5 g. and disappeared entirely when the dose was 0·25 g. a day. All except one of the patients had previously received mercurial diuretics as well as digitalis and a low-salt diet. On a daily morning dose of 0·5 g. of diamox together with a low-salt diet and digitalis, 11 of the patients were kept free from oedema and their weight more or less constant. The only beneficial effect in the other 2 patients, who had severe heart disease, was a less frequent need for mercurial injections. In the presence of anasarca and renal decompensation diamox, alone or combined with mercurials, had little diuretic effect; when ascitic fluid was removed, however, diamox appeared to be more efficacious, though supplementary mercurial injections were required. *I. Ansell*

MYOCARDIAL INFARCTION

488. **The Diagnosis of Posterior Myocardial Infarction**
L. Wolff, K. S. Mathur, and J. L. Richman. *American Heart Journal* [*Amer. Heart J.*] **46**, 21–37, July, 1953. 13 figs., 16 refs.

In a comparative study of vectorcardiographic and electrocardiographic findings in over 600 cases of myocardial infarction at the Beth Israel Hospital (Harvard Medical School), Boston, the vectorcardiogram indicated infarction of the posterior wall of the left ventricle in 104 cases. In 9 of these cases, in which the vectorcardiogram appeared to indicate a lesion confined to the upper part of the posterior wall of the left ventricle and the clinical picture was characteristic of infarction, the electrocardiogram provided no confirmation, even on extensive exploration of the thorax and oesophagus with unipolar leads. Further investigations were therefore undertaken to elucidate this discrepancy.

In an unselected series of 86 cases in which posterior myocardial infarction had been found post mortem a critical comparison was made between necropsy findings and the electrocardiographic diagnosis, with special reference to the position of the lesion in the posterior wall. It was found that in the interpretation of the electrocardiogram the diagnosis of posterior infarction had been missed in 39 of the 86 cases. A small lesion confined to the upper or middle part of the posterior wall of the left ventricle was present in 6 cases, and in 4 of these the diagnosis had been missed, while other causes of failure were the coexistence of a lesion of the anterior wall in 25 and of left bundle-branch block in 6.

It was thus confirmed that small infarcts occurring high in the posterior wall of the left ventricle do not, as a rule, produce characteristic signs on the electrocardiogram. When this area alone is affected the diagnosis of infarction may be missed altogether on ordinary electrocardiography, and probably in many more cases the existence of the posterior lesion is missed because of the simultaneous occurrence of an anterior lesion. The authors suggest that when electrocardiographic changes typical of acute anterior infarction are not accompanied by reciprocal changes in posterior leads, the coexistence of a posterior lesion should be suspected. *J. A. Cosh*

489. **The Ventricular Esophageal Electrocardiogram in the Diagnosis of Myocardial Infarction**
I. L. Rubin, M. P. Margolies, A. Smelin, and O. A. Rose. *American Heart Journal* [*Amer. Heart J.*] **46**, 38–48, July, 1953. 3 figs., 28 refs.

Leads III, aVF, and the oesophageal lead at ventricular level (EV) were compared in known cases of posterior myocardial infarction at the Bronx Veterans Administration and Montefiore Hospitals, New York. EV leads were recorded from points in the oesophagus at least 7·5 cm. below the lowest level at which intrinsic P deflections were obtained, this being regarded as the only reliable means of finding the ventricular level.

In the majority of 64 patients with posterior myocardial infarctions tracings from Lead EV resembled those from Lead aVF. However, in 8 cases there was a significant Q wave in Lead aVF but not in Lead EV, whereas in 5 the reverse was true, a Q wave of more than 25% of the size of the corresponding R wave and more than 0·04 second in duration being regarded as significant. Of 33 control subjects without infarction, significant Q waves were present in Lead EV in none, in Lead aVF in 5, and in Lead III in 18.

Thus Lead aVF was rather more consistent than Lead EV in indicating the presence of posterior myocardial infarction, but Lead aVF sometimes, and Lead III often, gave a "false positive" Q wave in normal controls, while Lead EV did not. *J. A. Cosh*

CHRONIC VALVULAR DISEASE

490. **Left Atrial and Pulmonary Capillary Venous Pressures in Mitral Stenosis**
R. G. Epps and R. H. Adler. *British Heart Journal* [*Brit. Heart J.*] **15**, 298–304, July, 1953. 7 figs., 13 refs.

Opinions differ as to how well the pulmonary capillary venous pressure (P.C.V.P.) agrees with the pressure in the left atrium, and as to the interpretation of the waves seen in P.C.V.P. tracings. Up to the present, simultaneous tracings from the two sites have been obtained only in the anaesthetized animal and in human subjects with an atrial septal defect.

In this paper the authors describe a method whereby a needle attached to the distal end of a metal bronchoscopic suction tube can be inserted directly into the left atrium at a point on the medial wall of the left main bronchus, 1 to 5 mm. below the carina. In combination with cardiac catheterization, consecutive tracings can be obtained of P.C.V.P. and left atrial pressure. In the 7 patients selected for study the correlation between the two recordings was extremely close, regardless of the height of the pulmonary arterial pressure. The P.C.V.P. tracings showed the character of a venous pulse wave, and the authors stress the importance of critical damping

to bring this out; even so, low pulmonary arterial pressures or extreme pulmonary vasoconstriction may obscure the venous wave. There is a good deal of lability in pressures with respiration and with minor variations in the resting state, and the rise in P.C.V.P. on bronchoscopy may be potentially dangerous. However, no complications occurred in the present study, which was carried out at the Brompton Hospital, London, on 6 patients with mitral stenosis and one with pure mitral incompetence.

A. Paton

491. **Studies in Cardiovascular Syphilis. III. The Natural History of Syphilitic Aortic Insufficiency**

B. Webster, C. Rich, P. M. Densen, J. E. Moore, C. S. Nicol, and P. Padget. *American Heart Journal* [*Amer. Heart J.*] **46**, 117–145, July, 1953. 10 figs., 12 refs.

A statistical analysis was carried out with the aim of determining the influence of various factors, considered singly, upon the course of syphilitic aortic incompetence in 1,020 patients, 711 of whom had first been seen at the Johns Hopkins Hospital, Baltimore, between 1925 and 1950, and 309 at the New York Hospital between 1930 and 1950. About 75% of the total were traced up to the time of the investigation. Owing to the lack of any controls, no attempt was made to evaluate specific therapy.

On the whole, over one-third of the total survived 10 years after being diagnosed. Survival was better among white men and negro women than among negro men, but this may have been due to sociological rather than to purely racial factors. Subjects engaged in heavy work at the time of diagnosis apparently survived better than those employed on light work or unemployed when diagnosed, presumably because the latter group included the more severely incapacitated. The survival rate among patients of all ages was considerably less than that of a similar group of the general population. In the first 2 years after diagnosis, younger patients (under 40) had a rather higher death rate than older patients, but thereafter the younger men did better than their elders. The presence of cardiac symptoms, of angina, and particularly of cardiac failure at the time of diagnosis affected the subsequent course unfavourably. Of the 632 patients who had died, the cause was considered to be cardiovascular disease in 75%. Of the 219 on whom necropsy was performed, 45 were found to have non-syphilitic heart disease.

J. A. Cosh

492. **Multivalvular Heart Disease and Simultaneous Surgical Correction**

H. E. Bolton, C. P. Bailey, W. L. Jamison, and K. V. S. Rao. *Journal of the International College of Surgeons* [*J. int. Coll. Surg.*] **20**, 1–10, July, 1953. 7 figs., 6 refs.

This short paper touches on some aspects of the recent rapid advances in the surgery of valvular lesions of the heart, with special reference to the treatment of "multivalvular" heart disease. Two techniques which have been developed by the authors at Hahnemann Hospital, Philadelphia, for dealing with incompetence of the mitral valve are described; in both a transventricular approach is made, the orifice in one case being sutured with pericardium, whereas in the other the aortic or septal leaflet of the valve is suspended by means of an artificial chorda tendinea, again made out of a strip of pericardium. The authors' technique of aortic commissurotomy is also briefly described, the risk of cerebral embolism during this operation is stressed, and the authors' method of avoiding this complication by control of the great vessels during manipulation is outlined.

Where lesions of both the aortic and mitral valve are present, the authors consider that the mitral disease should be dealt with first but that, if possible, both lesions should be treated at the same operation. The over-all mortality in the treatment of patients with multiple valvular lesions is necessarily higher than when only a single valve is affected, the authors' figure in a series of 29 such cases being 20·7% (6 deaths), but all but 2 of the survivors were improved by the operation.

J. R. Belcher

493. **Aortic Commissurotomy**

H. B. Larzelere and C. P. Bailey. *Journal of Thoracic Surgery* [*J. thorac. Surg.*] **26**, 31–66, July, 1953. 9 figs., 32 refs.

Since the successful development of mitral valvotomy the attention of the cardiac surgeon has been directed towards the aortic valve, but progress in this field has been slower for technical reasons. The authors, having explored the possibility of an approach to the valve from above as well as below, have now developed a transventricular technique in which an expanding dilator is passed through the wall of the ventricle, up the aortic outflow tract, and into the stenosed orifice. This has been successfully used in a number of cases at the Hahnemann Hospital, Philadelphia.

The most suitable type of aortic valvular lesion for surgical treatment is the acquired rheumatic form, the congenital and degenerative types not being likely to give satisfactory results. The authors' aim in treatment is to split the commissures joining the valve cusps fused by the disease process, and this cannot be done blindly for fear of rupturing the cusps with consequent regurgitation. They therefore developed a tri-fin expanding dilator on a swivel head which would adjust itself so that the blades lay in the remaining gaps between the fused cusps. This is threaded over a beaded guide-wire which is passed through the stricture like a filiform bougie. The operation is best carried out with the patient in the lateral position, which also allows the mitral valve to be explored, if necessary, and the great vessels leading to the brain to be isolated and compressed during the operation to prevent cerebral embolism. Out of the 42 cases in which aortic commissurotomy has been performed, mitral valvotomy was also carried out in 23. It is not always easy to decide which valve should be dealt with first; there are points in favour on both sides. The authors prefer on the whole to operate on the mitral valve first, unless there is severe aortic stenosis and mitral regurgitation, in which case the regurgitation may in part be due to the aortic obstruction.

A rapid anaesthetic induction is followed by a fifth-rib postero-lateral thoracotomy. The great vessels arising

from the aortic arch are isolated so that they can be compressed during cardiac manipulations, 2 minutes being the maximum permissible period of occlusion. The pericardium is widely opened, the aortic ring palpated, and the dilator set to a diameter just less than the external diameter of the aorta. A purse-string suture is placed in the wall of the left ventricle about 2 inches (5 cm.) from the apex and a control tourniquet attached to the suture ends. Through a tiny stab wound the guide-wire is passed into the heart and up towards the stenosis until, having traversed the stricture, it can be felt in the aorta. The incision is then enlarged to allow passage of the dilator, whose head is passed into the stenotic orifice and its position and alignment checked. The blades are then opened carefully several times, the instrument is withdrawn, the heart wound is sutured, and the pericardium loosely closed. The chief contraindications to operation are congestive failure which does not respond to treatment and great enlargement of the heart, which indicates advanced myocardial degeneration. Recent rheumatic fever and age over 50 are additional factors which make operation inadvisable.

The operation has been performed in 13 cases of isolated aortic valvular disease—7 with stenosis only and 6 with both stenosis and regurgitation—and in 29 cases of multivalvular lesions, of which there were 25 in which definite mitral stenosis was present; in 23 of these mitral commissurotomy was also performed. Of the 42 patients 7 died from various causes, including embolism and haemorrhage. Great improvement was noted in most of the survivors.

[This paper is one of great importance and should be studied in detail.] *T. Holmes Sellors*

CONGENITAL HEART DISEASE

494. **Congenital Tricuspid Atresia**

R. Astley, J. S. Oldham, and C. Parsons. *British Heart Journal* [*Brit. Heart J.*] **15**, 287–297, July, 1953. 7 figs., 19 refs.

The authors summarize their findings in 15 cases of tricuspid atresia and one case of tricuspid stenosis in 16 infants and children seen at the Children's Hospital, Birmingham. The presence or absence of transposition of the great vessels divided the cases into two anatomical groups of 7 and 9 patients respectively, and pulmonary stenosis was an added complication in 6 cases, 3 in each group.

In congenital tricuspid atresia the clinical findings are usually cyanosis, prominent pulsation of the neck veins, and often a rough systolic murmur in the left 3rd space. The electrocardiogram shows marked left axis deviation and left ventricular preponderance, and this is for all practical purposes a diagnostic finding. Radiology reveals two distinct groups of cases according to the degree of vascularity of the lung fields. Reduced pulmonary vascularity was present in 10 of the present cases (3 with transposition), and normal or increased pulmonary vascularity in 6 cases (4 with transposition). The cardiac silhouette shows concavity of the pulmonary segment, together with prominence in the upper part of the left lower segment, and a vertical border below this gives a rather square appearance. This square shape is determined by atrial enlargement. In the angiocardiogram there is immediate flow from the right auricle to the left so that a continuous band of opacity extends across the heart instead of the normal V-shape of the right heart in the frontal position. The space normally occupied by the right ventricle remains conspicuously empty. Angiocardiography, carried out in 7 cases, was found to be useful in confirming the diagnosis.

[This informative communication should be read in full.] *James W. Brown*

495. **Persistent Left Superior Vena Cava Draining the Pulmonary Veins**

F. Gardner and S. Oram. *British Heart Journal* [*Brit. Heart J.*] **15**, 305–318, July, 1953. 13 figs., 10 refs.

A persistent left superior vena cava is not an uncommon finding in children with congenital heart disease. This anomalous vessel usually carries venous blood from the upper part of the body to the right atrium via the coronary sinus and is of little functional importance. In the 4 cases seen at the Royal Free and King's College Hospitals, London, which are discussed by the authors the left superior vena cava received some or all of the pulmonary veins and passed arterial blood into the innominate vein and hence into the right atrium. This particular anomaly may be more common than is generally supposed, and may perhaps be amenable to surgical treatment.

From a clinical point of view there is evidence of an enormous left-to-right shunt with enlargement of the right ventricle and little or no cyanosis. Radiological investigation shows a wide, tulip-shaped shadow situated in the upper mediastinum and enveloping the aortic knuckle and pulmonary arc. The pulmonary arteries are large and show expansile pulsation. The electrocardiogram may show complete or incomplete right bundle-branch block. The diagnosis can be confirmed by cardiac catheterization, when arterial blood will be found in the innominate vein, and by angiocardiography. For the maintenance of life a large atrial septal defect is a necessary complementary abnormality, and the prognosis depends in part upon this and in part upon the amount of blood diverted to the right atrium. Of the 4 patients described, 2 are alive at the age of 24. The scope of surgical correction, which was attempted in one case but found impracticable, is briefly discussed. *James W. Brown*

496. **The Syndrome of Patent Ductus Arteriosus with Pulmonary Hypertension**

H. Hultgren, A. Selzer, A. Purdy, E. Holman, and F. Gerbode. *Circulation* [*Circulation (N.Y.)*] **8**, 15–35, July, 1953. 6 figs., bibliography.

A study of 8 cases of patent ductus arteriosus associated with marked pulmonary hypertension is reported in this paper from Stanford University, San Francisco. The methods of investigation used are described in detail. In 4 cases varying degrees of cyanosis and polycythaemia

were present, with evidence of reversal of flow through the ductus. At necropsy on one of these patients the diffusibility of kerosene through the pulmonary vascular field was shown to be markedly diminished, radiography after injection of opaque medium into the pulmonary artery revealed obliteration of its finer terminal branches, and histological examination showed marked structural changes in the smaller pulmonary arterioles. In the remaining 4 cases no evidence of reversed shunt was found, but atypical clinical features were present, together with marked pulmonary hypertension; in 2 of these the ductus was tied successfully, but the other 2 patients died of congestive heart failure.

The authors believe this condition to be commoner than is generally realized, and perhaps comparable in incidence to Eisenmenger's complex, with which it may be confused. Other conditions from which it must be differentiated are atrial septal defect with pulmonary hypertension and primary pulmonary hypertension. The symptoms, signs, and results of investigation in the authors' cases are fully described. The most important aid to the diagnosis of patency of the ductus with reversed shunt is the determination of the oxygen content of samples of blood taken simultaneously from the brachial and femoral arteries at rest and during exercise. Cardiac catheterization is necessary to detect a patent ductus without reversed shunt. The highest pulmonary arterial pressure and the lowest calculated pulmonary blood flow were found in the cyanotic cases. After ligation of the ductus in one (non-cyanotic) case the pulmonary arterial pressure remained abnormally high.

The major cause of the pulmonary hypertension in these cases is an increase in the vascular resistance of the lung, and the possible causes of narrowing of pulmonary vessels are discussed, there being some evidence in favour of multiple, repeated pulmonary emboli or a primary pulmonary arteritis. [This problem has also been fully discussed by Dammann *et al.* (*Bull. Johns Hopk. Hosp.*, 1953, **92**, 128; *Abstracts of World Medicine*, 1953, **14**, 213).] *R. S. Stevens*

497. **The Morbid Physiology of Eisenmenger's Complex.** (Physiopathologie du complexe d'Eisenmenger)
P. Soulié, G. Voci, J. Carlotti, and F. Joly. *Archives des maladies du cœur et des vaisseaux* [*Arch. Mal. Cœur*] 46, 481–502, June, 1953. 5 figs., 29 refs.

This paper is based on observations made at the Hôpital Lariboisière, Paris, on 12 patients with Eisenmenger's syndrome, 5 being female and 7 male, and their ages ranging from 6 to 28 years. Apart from routine cardiological investigations, all patients underwent cardiac catheterization and 10 angiocardiography. In most of them the left heart could be explored by the catheter by one of several routes. In all cases the systolic pressure in the right ventricle and pulmonary artery was the same and equalled that in the systemic circulation, the systolic as well as the diastolic pressure in the pulmonary artery being greatly increased. The arteriolar resistance in the pulmonary circulation was considerably raised, however, and the pulmonary capillary pressure was normal, the pulmonary capillaries thus being protected from any damaging effect of the pulmonary arterial hypertension, and the equilibrium necessary for survival being maintained in the circulation as a whole. In 4 patients in whom the oxygen saturation of arterial blood varied between 80 and 90% at rest, inhalation of pure oxygen raised it within 5 minutes to 94·5 or 95%. In 3 of these cases exercise had little or no effect on the ventilation quotient and reduced the oxygen saturation of the peripheral blood by about 3%; in a further case in which the oxygen saturation of the peripheral blood was normal at rest, exercise had no effect.

From these observations the authors conclude that in the evolution of Eisenmenger's syndrome two successive and distinct stages can be recognized. (1) In the acyanotic stage the oxygen saturation of the peripheral blood is normal at rest and after exercise, and the abnormal origin of the aorta, overriding a septal defect, is without any functional significance; the intracardiac shunt is exclusively from left to right, the minute volume in the pulmonary artery is increased and exceeds that in the periphery, and the resistance in the pulmonary arterioles is increased, but is less than the peripheral resistance. (2) In the cyanotic stage the oxygen saturation in the peripheral blood is below normal, and it is shown that this is exclusively due to the intracardiac right-to-left shunt, since the oxygen saturation of the blood in the pulmonary veins is normal. This reversal in the direction of the intracardiac shunt is largely due to a change in the relation between the arteriolar resistances of the pulmonary and peripheral circulations, that of the former equalling or exceeding that of the latter at this stage in most cases. It is suggested that these differences are due to the different degrees of overriding of the aorta, and the different amounts of venous blood consequently admitted into the aorta, in different cases. It is emphasized that absence of cyanosis does not exclude the presence of Eisenmenger's syndrome; in such cases the diagnosis can be made only by catheterization.

[The authors of this paper present a closely argued evaluation and interpretation of the various haemodynamic, clinical, and morbid physiological features of this congenital malformation; those interested in the condition will find the study of the original paper rewarding.] *A. Schott*

498. **The Angiocardiogram in Fallot's Tetralogy**
J. B. Lowe. *British Heart Journal* [*Brit. Heart J.*] **15**, 319–329, July, 1953. 14 figs., 24 refs.

The angiocardiograms of some 50 patients diagnosed at the National Heart and Brompton Hospitals, London, as suffering from the tetralogy of Fallot are reviewed in this paper from the Institute of Cardiology, London. The author finds that pulmonary stenosis does not cause delay in the filling of the pulmonary arteries, and poor opacification of these vessels is exceptional. The actual site of pulmonary stenosis is rarely clearly seen, but a clue is afforded by the reduction in the calibre of the pulmonary tree in some cases, while in others there is no visible abnormality of the pulmonary arteries. In 18 cases in which the angiocardiographic findings were correlated with the findings at surgical operation or at

necropsy, the site of stenosis was clearly demonstrated by the angiocardiogram in 3. In another 8 cases the site of stenosis was suggested by indirect evidence, but in 7 cases there was no indication whatsoever of the site of the obstruction.

The author discusses the difficulties of differential diagnosis between the tetralogy of Fallot, the Eisenmenger complex, and pulmonary stenosis with closed ventricular septum and a reversed interatrial flow.

James W. Brown

499. **Necropsies in Some Congenital Diseases of the Heart, Mainly Fallot's Tetralogy**

W. D. BRINTON and M. CAMPBELL. *British Heart Journal* [*Brit. Heart J.*] **15**, 335–349, July, 1953. 10 figs., 11 refs.

There were 55 necropsies at Guy's Hospital in 1947–50 on patients with congenital heart disease. Twenty-five of these were examples of simple Fallot's tetralogy and have been described fully. The general picture is very similar in each case though there is a good deal of variation in detail.

A functional defect of the atrial septum, about 9 by 5 mm., is present in more than one-third, but does not seem to make any difference to the clinical picture. The ventricular septal defect is nearly always just below the valves and is bounded below by a saddle-shaped ridge of muscle clothed with smooth endocardium: its size corresponds with the size of the heart and is commonly between 10 and 16 mm. in transverse diameter.

The aorta always over-rides this except in the rarer cases where it arises entirely from the right ventricle, and the degree to which this happens varies between one-quarter and seven-eighths, and averages three-fifths, i.e. more over the right than over the left ventricle. The right ventricle is always hypertrophied and is commonly 50% thicker than the left, averaging nearly 12 mm. against 8 mm. for the left.

The pulmonary trunk is smaller than the aorta, generally between 40 and 80% of its size, instead of being about the same; the average diameters were 10 mm. and 17 mm. Taking our figures from a more extensive series the stenosis is infundibular alone in one-half, infundibular and valvular in one-sixth, and valvular alone in one-third. When it is infundibular, the site is commonly from 5 to 25 mm. below the valve and is sometimes multiple: there is generally a fibrous ring, but the whole tract is narrower and under-developed. When it is valvular it has the familiar appearance of a conical diaphragm with a small central orifice, and has developed from two cusps or from three cusps in about equal numbers of cases.

The clinical picture of these patients with Fallot's tetralogy has been referred to shortly, and the commoner *x*-ray appearances have been described. The classical sabot-shaped heart is not very common except in infants and there is much variation in the shape and appearance of the heart, but most resemble one of four types illustrated. Right ventricular enlargement is generally obvious on radioscopy, but rotation of the heart may simulate enlargement of the left ventricle as well. Right ventricular preponderance in the electrocardiogram is more constant and more reliable.

Six other patients had the general features of Fallot's tetralogy but with pulmonary atresia instead of stenosis. Seven had pulmonary valvular stenosis with a closed ventricular septum: all but one of these had a right-to-left shunt through the atrial septum. Two had Ebstein's anomaly of the tricuspid valve. These three groups have been described elsewhere.

Six others had an atrial septal defect. Three of these, two of whom had mitral stenosis also, lived to middle age and the fourth with a very large defect was hardly inconvenienced till she was 49 and lived to 63 years of age. The other two with very large defects and great right ventricular hypertrophy died in infancy.

There were single examples of tricuspid atresia and of atresia of the aortic arch: both these died in infancy. One patient had an unusually primitive type of heart with a single ventricle, infundibular stenosis, and transposition of the aorta and pulmonary trunk. Six others had transposition, three with and three without pulmonary stenosis. Most of them died in infancy, but one with pulmonary stenosis lived 25 years. One had in addition isolated dextrocardia and another had transposed abdominal viscera.—[Authors' summary.]

BLOOD VESSELS

500. **Aortic Homografting. A Report of Six Successful Cases**

R. C. BROCK. *Guy's Hospital Reports* [*Guy's Hosp. Rep.*] **102**, 204–228, 1953. 18 figs., 20 refs.

The use of a homograft in 6 cases of aortic reconstruction is described, the graft in each case being undertaken for what would otherwise have proved a fatal condition. In 3 cases of coarctation of the aorta where the stricture was long or complicated by aneurysm the results were good. The author states that continuity of the aortic lumen could not have been achieved had not a graft been used; therefore, grafts should always be at hand when an operation is being performed for coarctation of the aorta, and should be used when there is a long segment of narrowing, a rigid and inelastic aorta even if the gap is narrow, aneurysm of the aorta or of the intercostal arteries, or surgical injury to the aorta or its major branches.

In the fourth case in the series there was aneurysm of the descending aorta in association with coarctation; a graft measuring 12·5 cm. was inserted, and the patient made a good recovery. In the fifth case a large aneurysm of the abdominal aorta was resected and a graft successfully inserted from just below the renal arteries to the origin of the two common iliac arteries. An insidious thrombosis of the aortic bifurcation (Leriche's syndrome) was present in the sixth case, and a graft was inserted into unhealthy atheromatous aorta from just below the renal arteries to the common iliac vessels after clot had been teased out of the upper and lower parent vessels. After operation the distal pulses were good and the claudication improved. Unfortu-

nately a leak in the upper anastomosis gave rise to a false aneurysm which ruptured 6 months after the operation.

The author believes that there is evidence to support the contention that an arteriogram taken immediately before or 6 months after a grafting procedure may be responsible for an increase in thrombosis.

Peter Martin

501. **Some Complications of Temporal Arteritis**
D. KENDALL. *British Medical Journal* [*Brit. med. J.*] **2**, 418–420, Aug. 22, 1953. 1 fig., 11 refs.

The author discusses the complications of temporal arteritis, a condition first fully described by Horton *et al.* (*Proc. Mayo Clin.*, 1932, **7**, 700). He suggests that the term " temporal arteritis " is inadequate, since there is widespread arteritis affecting predominantly the branches of the external and internal carotid vessels. The fundamental aetiology of the condition is unknown. Detailed histories are given of 9 patients seen at the Royal Surrey County Hospital; the patients' ages ranged from 66 to 82, 6 of them being in the 8th decade. Severe headache or head pain was present in all, and in 8 there was (usually temporal) arterial thrombosis. The diagnosis was made clinically, although one case was confirmed by biopsy. In 4 cases complete blindness occurred, in 2 others there was loss of sight in one eye, and in 2 ocular palsies were present. There were also one case of necrosis of the scalp and nasal septum and one of severe vertigo. Fever, wasting, and a raised erythrocyte sedimentation rate were also noted. Some recovery of vision occurred in one case, and return of peripheral circulation in 2 cases. In treatment, salicylates were found of value, at least in the relief of symptoms, but there was considerable relief from pain after biopsy of the temporal artery in the one case where this was performed. It is pointed out that there may be a considerable interval between the original symptoms and the loss of vision.

[This high proportion of ocular complications raises the question of preventive treatment. Cortisone and corticotrophin (ACTH) have been found to give relief of symptoms. If ocular damage occurs, the use of these hormones or of anticoagulants may be considered, bearing in mind the risk of total blindness and the possibility of recovery of circulation in this self-limiting though long-drawn-out disease.] *W. A. Bourne*

502. **Aging Processes in the Arterial and Venous Systems of the Lower Extremities**
M. D. PAREIRA, F. P. HANDLER, and H. T. BLUMENTHAL. *Circulation* [*Circulation (N.Y.)*] **8**, 36–43, July, 1953. 8 figs., 19 refs.

An investigation is reported from St. Louis University School of Medicine in which the arteries and veins of 45 lower limbs were dissected, 36 of which had been amputated at the mid-thigh because of gangrene resulting from vascular occlusion due to atherosclerosis in patients of whom the youngest was a diabetic of 47. The remaining 9 limbs were from younger subjects and had had to be amputated because of trauma or neoplasm. Segments were taken for histological examination from the popliteal artery 1 cm. above the popliteal fold, from the anterior and posterior tibial arteries 1 cm. distal to their origin and also 1 cm. above the malleolar line, from the dorsalis pedis artery about 3 cm. below the malleolar line, and from the skin and digital artery about 1 cm. distal to the interdigital web. Specimens of gastrocnemius muscle were also taken for the study of its nutrient arteries. From each of these specimens 3 sections were prepared, one being stained with haematoxylin and eosin and one for elastic tissue, and the third being incinerated and its ash examined. In addition, the limb vessels of 6 subjects over 50 were examined and the internal diameter of vessels without occlusive vascular disease measured. From these data the internal hydrostatic pressure at various levels was worked out by means of Burton's formula.

From their findings in these and previous investigations the authors describe the changes which take place in the vessels of the lower limb with increasing age. At birth the endothelial lining of the arteries lies on the internal elastic lamella, but after the age of 20 these become separated by collagen and elastic fibres, though the elastic tissue tends to be less prominent in older subjects. Calcification appears first as a deposit on the elastic fibrils and may eventually progress to bone formation. These changes are found in decreasing severity as the vessel proceeds distally, being comparatively minor in the digital and muscular arteries. The tibial and popliteal veins were also examined and showed a similar condition of endophlebohypertrophy with proliferation of collagen and elastic fibres and deposition of calcium on the elastic elements.

A close correlation was found between calcification and atheromatous plaque formation and the hydrostatic pressure at any point. On the other hand thrombi were most frequently found in the tibial arteries despite the higher incidence of plaques and calcification in the popliteal arteries. *Peter Harvey*

503. **Major Venous Ligation in the Treatment of Post-phlebitic Sequelae**
A. M. BOYD, B. N. CATCHPOLE, R. P. JEPSON, and S. S. ROSE. *Lancet* [*Lancet*] **2**, 113–116, July 18, 1953. 6 figs., 9 refs.

During recent years increasing interest has been taken in the operation of ligation of a major vein in cases of long-standing deep venous thrombosis, and in the present paper from the University of Manchester, the authors report the results of this procedure in 42 cases of venous incompetence following thrombophlebitis. In all the cases phlebography was carried out and venous pressure recorded both before and after the operation. At the time of ligating the vein all ulcers were excised and grafted. Either the femoral or the popliteal vein was tied; in 3 cases both veins were tied. After operation the limb was supported by an elastic or crêpe bandage and the patient told to avoid standing for long periods at a time.

The patients were seen at 3- to 6-monthly intervals for at least 3 years. In all the cases in which the ligature had been placed on the popliteal vein there was a marked

increase in venous pressure on exercise, indicating increased venous incapacity in the limb. Phlebograms showed gross dilatation of collateral veins around the site of ligation, the veins appearing to be valveless. There was clinical improvement in a few cases, however, and ulcers remained healed, but the authors attribute this to simultaneous ligation of an incompetent saphenous vein, the grafting of ulcers, the correction of general nutrition, and, probably most important, the detailed after-care and attention. They conclude that there is no place for deep-vein ligation in the treatment of the post-phlebitic syndrome.

[Most surgeons in Britain have reached the same conclusions. The only efficient ambulant treatment is firm elastic support, when all ulcers due to the post-phlebitic syndrome will heal.] *Peter Martin*

SYSTEMIC CIRCULATORY DISORDERS

504. **Headache and Hypertension**
I. McD. G. Stewart. *Lancet* [*Lancet*] **1**, 1261–1266, June 27, 1953. 1 fig., 24 refs.

The clinical significance of symptomatic headache in hypertension was studied at the United Bristol Hospitals in 200 consecutive patients with a diastolic blood pressure of 120 mm. Hg or higher while at rest in the recumbent position. In the majority of the patients the headaches were considered to be the result of anxiety. No fewer than 104 of the patients were unaware that they had a raised blood pressure, and only 17 of these would admit to having headaches. A characteristic pattern of organic hypertensive headache could be defined only with difficulty. Although this type of headache was not common, it had certain distinguishing features: it was severe, resembling migraine, with onset soon after the blood pressure began to rise; it was of short duration, though perhaps recurrent, and was not related to the rise in diastolic blood pressure or to the left ventricular state. Organic headache was noted relatively often within the syndrome of malignant hypertension and also in women at the menopause. The author draws attention to the fallacy of "acclaiming any treatment of hypertension in virtue of its alleged cure of headache". This symptom can seldom be regarded as a reliable diagnostic or prognostic aid in hypertension.
J. L. Lovibond

505. **The State of the Receptor Apparatus of the Heart in Essential Hypertension.** (Состояние рецепторного аппарата сердца при гипертонической болезни)
A. F. Kiseleva. *Архив Патологии* [*Arkh. Patol.*] **15**, 22–26, July–Aug., 1953. 3 figs., 19 refs.

In 35 cases of essential hypertension the heart was examined histologically, with particular attention to the atrial walls and the interatrial septum. The stains used were haematoxylin–eosin, picrofuchsin, and the silver impregnation method. Special attention was paid to the state of sensory nerve endings, the so-called receptor apparatus. The earliest abnormality observed was increased argyrophilia without any obvious morphological changes. Then irregular elongated and bulbous thickenings appeared along the course of the terminal fibrils followed by fragmentation or complete disintegration of the fibrils with a loss of affinity for silver, and in some places irregular regeneration of the fibrils.

These changes are said to resemble those demonstrated in experimental hypoxia. The author proceeds on the assumption that essential hypertension is a disease of nervous origin due to "cortical derangement", and that the peripheral nervous system, especially its afferent part, also plays an important role in the aetiology of the condition. *A. Swan*

506. **Results of Dorso-lumbar Sympathectomy in the Treatment of Essential Hypertension. A Review of 80 Cases.** (Resultados de la simpatectomía dorsolombar en el tratamiento de la hipertensión arterial esencial. Revisión de 80 casos)
L. Castañeda and L. Méndez. *Archivos del Instituto de cardiología de México* [*Arch. Inst. Cardiol. Méx.*] **23**, 27–48, Feb. 28, 1953. 7 refs.

The results of dorso-lumbar sympathectomy carried out in 80 cases of essential hypertension are reported from the National Institute of Cardiology of Mexico. The operative technique was that of Smithwick. The great majority of the patients were between 35 and 55 years of age, though 3 were under 30 and one was 63. In 57 (77%) the systolic pressure was over 200 mm. Hg before operation, and in 29 (30%) the blood pressure remained above this level afterwards. Diastolic pressure was over 130 mm. Hg in 64 (85·7%) out of 74 before and in 24 (32·4%) after operation. Heart failure of some degree was present before operation in 58 (74·7%) out of 78 cases and in 12·8% of these it was severe. The heart failure disappeared in 23 cases (39·6%) and a considerable improvement was seen in a further 19 (32·7%). During a follow-up period of 7½ years, 17 patients died—more than half of them from a cerebral vascular accident, indicating that the operation increases the risk of this complication.

It is concluded that heart failure, especially when medical treatment has failed, is the main indication for operation in essential hypertension, and that only in such cases does operation offer a good hope of improvement. Retinal changes may also constitute an indication. Long-term improvement in the blood pressure was not often seen. *Donald McDonald*

507. **Orally Administered Hexamethonium Chloride in Hypertension**
J. H. Moyer, S. I. Miller, and R. V. Ford. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **152**, 1121–1129, July 18, 1953. 4 figs., 8 refs.

The effect on hypertension of oral administration of hexamethonium chloride, an effective autonomic ganglionic blocking agent, is described in this paper from Baylor University, Houston, Texas. A total of 120 hypertensive patients were divided into three groups according to the diastolic pressure as follows: Group 1 (29 cases) diastolic pressure between 100 and 120 mm. Hg; Group 2 (58 cases), 120 to 140 mm. Hg; and Group 3

(33 cases) over 140 mm. Hg. In one-third of the patients there was evidence of impaired renal function and in one-third cardiac failure. Malignant hypertension was present in 20, and cerebral vascular involvement in 22.

The initial dose of hexamethonium chloride was 250 mg. given 4 times daily with meals to diminish gastric disturbance; this dose was gradually increased until the blood pressure fell or the limit of tolerance was reached. To avoid orthostatic dizziness the dose was subsequently adjusted so that the blood pressure in the erect position was not less than 150/90. Side-effects were seldom so severe as to prohibit treatment, but in 3 patients the dose necessary for a satisfactory hypotensive effect resulted in retention of urine and the drug had to be withdrawn.

A satisfactory hypotensive response was obtained in 25 patients in Group 1, 49 in Group 2, and 29 in Group 3. Of the patients with headache and angina over three-quarters obtained relief, while symptoms improved in two-thirds of the patients with cardiac failure. Patients with malignant hypertension proved very resistant to therapy. In 9 azotaemic patients a fall in blood pressure was accompanied by a rise in the blood urea level. There were 8 deaths in the series, all in patients who did not respond to the treatment.

In 28 of the 44 patients observed for more than a year the hypotensive effect was maintained, and there was no evidence of tolerance to the drug. Cerebral blood flow and oxygen uptake were reduced in the upright posture in one patient, and in another renal plasma flow and glomerular filtration rate fell initially when the blood pressure was reduced, but returned to normal even though the low blood pressure was maintained.

D. Weitzman

508. **The Acute Effects of Hexamethonium on Renal Hemodynamics in Normotensive and Hypertensive Human Subjects**

L. C. Mills and J. H. Moyer. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **226**, 1–15, July, 1953. 3 figs., 22 refs.

The authors analyse in detail the acute changes in renal haemodynamics observed after intravenous injection of hexamethonium chloride or bromide in doses of 5 to 75 mg. in 19 patients with hypertensive vascular disease and in 12 normotensive control patients at the Jefferson Davis Hospital (Baylor University), Houston, Texas. All showed some fall in blood pressure in the supine position. The patients could be divided into two groups, depending upon the change in renal vascular resistance. In Group I (10 controls and 7 hypertensive patients with severe renal damage), in which renal vascular resistance remained unaltered or increased, the hypertensive patients showed a mean fall in blood pressure to an average of 83% of the control level, and at the time of maximal reduction of blood pressure the urine flow fell to 35%, the glomerular filtration rate (G.F.R.) to 74%, and the renal blood flow (R.B.F.) to 73% of the control levels. Within one hour, renal function tended to improve again despite continued reduction of blood pressure. In Group II (2 control patients and 12 hypertensive patients of whom 6 had good and 6 had poor renal function) the renal vascular resistance fell at the time of maximum blood-pressure reduction. In these 12 hypertensive patients the mean blood pressure was reduced to 80% of the control level, the G.F.R. fell to 88%, and the R.B.F. to 98% of control values with, in contrast to Group I, a fall in the filtration fraction. Again renal function tended to improve despite continued reduction of blood pressure. In 2 patients in Group II the renal extraction of *p*-amino-hippurate was shown to remain within normal limits following administration of hexamethonium.

The renal haemodynamic response to hexamethonium is probably determined in a complex fashion by the pre-existing sympathetic renal vasoconstriction, organic renal vascular change, extent of ganglionic blockade, degree of blood-pressure reduction, and autonomous renal haemodynamic readjustment. The authors emphasize the importance of making serial determinations of the blood urea level in patients with renal disease who are receiving hexamethonium therapy. *K. G. Lowe*

509. **The Nature and Treatment of the Coeliac-plexus Reflex in Man**

B. H. Smith. *Lancet* [*Lancet*] **2**, 223–227, Aug. 1, 1953. 5 figs., 19 refs.

During surgical operations on the upper abdomen under light anaesthesia traction on the viscera sometimes elicits a sudden precipitous fall in blood pressure without a corresponding change in pulse rate. Burstein and Rovenstine, who first drew attention to this phenomenon in 1937, called it the " coeliac-plexus reflex " and concluded from experiments on dogs that it was due to increased sympathetic tone. Neostigmine was said to abolish the established reflex and also to prevent its occurrence. The author, working at the Queen Elizabeth Hospital, Birmingham, has observed the reflex on 10 occasions—8 times during gastrectomy, once during cholecystectomy, and once during cholecystoduodenostomy. One patient collapsed and died during mobilization of the duodenum.

Stimulation of the vagus nerve, experimentally or by surgical manipulations in the thorax and neck, may produce a condition similar to that of the coeliac-plexus reflex, which responds to the intravenous administration of atropine. This drug was therefore given to 6 of the 10 patients developing the reflex, and in all 6 there was an excellent response. This strongly suggests that the reflex is due to an increase in vagal rather than sympathetic tone, with a consequent reduction in stroke volume, the pulse rate being kept constant by means of the Bainbridge reflex. Preventive measures, which should be taken especially in cases in which a slow preoperative pulse rate suggests the presence of high vagal tone, include the use of atropine rather than scopolamine for premedication, the avoidance of cyclopropane, which increases vagal tone, and the use of gallamine in preference to D-tubocurarine, which blocks the vagus less well.

[It may be that the ganglion-blocking agents such as hexamethonium will have a greater part to play in the future in preventing shock from reflex disturbances during operation.] *B. L. Finer*

Haematology

510. **Renal Calculi and Uremia as Complications of Lymphoma**
A. S. WEISBERGER and L. PERSKY. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **225**, 669–673, June, 1953. 1 fig., 15 refs.

When therapeutic agents capable of producing rapid and extensive nuclear destruction are given to patients with lymphoma, the breakdown of nucleoproteins leads to increased formation of uric acid, but it is not generally recognized (although some cases have been reported) that uraemia may result from obstruction of the collecting tubules and ureters by precipitation of urates and uric acid.

The records of 283 patients with lymphoma admitted to the University Hospitals of Cleveland, Ohio, in a 10-year period were examined; of these patients, 15 (5·3%) had had renal calculi, uric acid calculi having been found in 7 (2·5%). No calculi were noted in a control series of 100 patients with metastatic disease other than lymphoma. The incidence of uric acid calculi in the general hospital population was 0·07%. In this series none of the 47 patients with Hodgkin's disease developed calculi. The reaction of the urine of all patients who developed calculi was acid.

Prophylaxis and treatment are discussed, and 2 cases are described. *E. G. Rees*

511. **Eosinophilic Leukaemia.** (Leucemia eosinofila)
A. MORELLI and C. MAUREA. *Haematologica* [*Haematologica*] **37**, 435–498, 1953. 24 figs., bibliography.

The authors review the literature of eosinophilic leukaemia, about 70 cases of which have been reported since 1912. They then describe the case of a man of 47 who was admitted to the Medical Institute of the University of Rome with myeloid leukaemia. The total leucocyte count ranged between 6,000 and 62,000 per c.mm.; the number of neutrophil granulocytes was always within normal limits, never exceeding 5,000 per c.mm., but that of eosinophils and their precursors varied between 5,000 and 50,000 per c.mm. After an injection of adrenaline the eosinophil count increased while the neutrophil count was unchanged. In smears of the bone marrow 16% of the cells seen were eosinophils and 25% eosinophil myelocytes. In smears of splenic-puncture material 70% of the cells were eosinophils, and in material aspirated from lymph nodes the proportion was 40%. Treatment with 650 mg. of ACTH daily for 13 days did not materially alter the blood picture, but the administration of nitrogen mustard, and later of urethane, reduced the number of all types of leucocyte in the circulating blood. Terminally, the leucocyte count rose to 76,000 and that of the eosinophils to 31,000 per c.mm. Although necropsy was not permitted, it was concluded that this was a true case of eosinophilic leukaemia. *E. Neumark*

512. **A Study of Bacteria Implicated in Transfusion Reactions and of Bacteria Isolated from Blood Products**
M. PITTMAN. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **42**, 273–288, Aug., 1953. 1 fig., 45 refs.

In this paper from the Microbiological Laboratory of the U.S. National Institutes of Health, Bethesda, Maryland, the author reports the results of a study of the organisms present in 98 cultures of blood and blood products and 11 of vaccines and antigens. Of these, 13 were cultured from the blood or blood products implicated in 18 severe or fatal blood-transfusion reactions; it was found that 8 of these organisms were types of *Pseudomonas* other than *Ps. aeruginosa*, 2 *Paracolobactrum aerogenoides*, and 3 *Bacterium coli freundii*. In a study of the optimum temperature range for growth, it was shown that all the strains associated with reactions, and all other Gram-negative rods, grew at the usual blood-storage temperatures. Of the pseudomonads, all grew at the lowest temperature, some did not grow at all at 37° C., and others very poorly at this temperature.

In cultures of blood products not associated with transfusion reactions micrococci predominated in those of plasma and albumin and were of several species. Streptococci occurred only in plasma. Gram-negative rods, spore-forming bacilli, and diphtheroids were also isolated. The temperature range for growth of the Gram-positive bacteria was, on the whole, higher than for the Gram-negative rods, although a few did grow at 10° C.

The author ends with a discussion of the importance of non-pathogenic bacteria as a source of contamination of stored blood and blood products, the use of a correct temperature for sterility tests, and the correct identification of the contaminants. *R. F. Jennison*

HAEMORRHAGIC DISEASES

513. **Diagnosis of " Sedormid " Purpura**
D. K. GRANT. *British Medical Journal* [*Brit. med. J.*] 2, 128–131, July 18, 1953. 8 refs.

The author, working at the Royal Prince Alfred Hospital, Sydney, has attempted to assess the value of tests carried out *in vitro* in the diagnosis of purpura thought to be due to the hypnotic " sedormid " (allyl-*iso*propylacetylurea).

In 4 out of 6 patients suffering from purpura after taking sedormid clot retraction was significantly reduced, but only in the early stages of the purpura, the retraction becoming normal within a few days. In one of these patients there was a temporary reduction in clot retraction a month after it had become normal. In the other 2 patients clot retraction was normal. In 5 patients a patch test with sedormid in propylene glycol produced

no skin reaction. When a test dose of sedormid was given to 2 patients 8 and 20 months after the drug had last been taken no purpuric manifestations were observed.

The author concludes that since sensitivity to sedormid may be of short duration, tests should be performed *in vitro* as soon as a provisional diagnosis of purpura has been made, and preferably when the purpura is obvious.

D. G. Adamson

514. **Electron Microscopic Studies of the Action of Thrombin on Blood Platelets**

E. De Robertis, P. Paseyro, and M. Reissig. *Blood* [*Blood*] **8**, 587–597, July, 1953. 8 figs., 12 refs.

Preparations of human blood platelets, made on parlodion films by means of the technique described by Bernhard *et al.* (*Presse méd.*, 1950, **58**, 472; *Abstracts of World Medicine*, 1950, **8**, 343), were examined under the electron microscope at the Institute of Biological Research, Montevideo, and their appearance studied after exposure to the action of bovine thrombin. A commercial preparation of thrombin was used initially at concentrations of 25 and 50 units per ml. in Tyrode solution, the preparation being immersed in the solution and kept at 35° C. for 5 to 30 minutes. The purified bovine thrombin of Seegers, dissolved in Tyrode solution in various concentrations between 2·5 and 50 units per ml., was used in later experiments, the platelet films being all incubated for 20 minutes with this preparation. Lysis of the platelets occurred with both samples of thrombin, the process [which is well illustrated in the numerous electron photomicrographs reproduced] starting with the gradual disintegration from without inwards of the hyalomere, leaving long fibrils, woven together and apparently consisting of rows of microvesicles, which themselves finally split up. The internal zone or granulomere then changes into a round, opaque, amorphous mass, which, in its turn, ultimately becomes lysed, the final picture being one of disintegrating opaque bodies and scattered microvesicles.

It is of interest to note that these effects could be obtained with a thrombin concentration as low as 2·5 units per ml., which may be present in normal clotting blood.

John Murray

515. **Studies on Platelets. X. Morphologic Characteristics of Megakaryocytes by Phase Contrast Microscopy in Normals and in Patients with Idiopathic Thrombocytopenic Purpura**

A. V. Pisciotta, M. Stefanini, and W. Dameshek. *Blood* [*Blood*] **8**, 703–723, Aug., 1953. 39 figs., 30 refs.

At the New England Center Hospital, Boston, megakaryocytes were studied by phase-contrast microscopy in 9 cases of idiopathic thrombocytopenic purpura and in 14 subjects in whom the platelet count was normal. In the patients with idiopathic thrombocytopenic purpura there was an increase in the total number of megakaryocytes, with immature cells predominating and apparently producing large and bizarre platelets. Other significant findings were lack of platelet formation in adult forms—as judged by the absence of granularity, refractile granules, pseudopod formation, and rupture of the cell membrane—and marked cell degeneration. After splenectomy there was a rapid maturation of megakaryocytes. In the healthy subject administration of plasma from a patient with a high-titre platelet agglutinin induced similar changes in the megakaryocytes.

Marjorie Le Vay

516. **Haemophilia B. Two Cases of a Familial Haemorrhagic Disorder due to Lack of a New Clotting Factor (the " Christmas " Factor).** (Die Hämophilie B. Zwei familiäre Fälle der Bluterkrankheit bedingt durch den Mangel eines neuen Gerinnungsfaktors (" Christmas Factor "))

R. Cramer, M. Matter, and A. Loeliger. *Helvetica paediatrica acta* [*Helv. paediat. Acta*] **8**, 185–201, June, 1953. 7 figs., 26 refs.

From the Children's Clinic, University of Zürich, the authors describe 2 cases, in boys aged 6 and 9 respectively, of sex-linked haemophilia which differed from the common form. These patients did not lack the antihaemophilic globulin. The coagulation defect could be corrected *in vitro* by addition of plasma from normal subjects and also from haemophilic patients; serum had the same effect. The correcting factor seemed to be identical with the antihaemophilic globulin (" Christmas factor ") described by Biggs *et al.* (*Brit. med. J.*, 1952, **2**, 1378; *Abstracts of World Medicine*, 1954, **15**, 50).

Kate Maunsell

ANAEMIA

517. **Bone-marrow Therapy in Malarial Anaemia.** (Опыт парэнтерального применения костного мозга в комплексном лечении малярийной анемии)

T. A. Gusenbeili. *Клиническая Медицина* [*Klin. Med.* (*Mosk.*)] **31**, 71–74, June, 1953. 8 refs.

The author describes a method of treatment of severe anaemia due to malaria with intramuscular injections of the patient's own sternal marrow in quantities of 1 to 2 ml. [the intervals are not stated]. The response is rapid and adequate, and there are no side-effects. Blood grouping is found to be unnecessary, even when the marrow of another person is used. The marrow of the patient, which is often of the pro-erythroblastic type, rapidly becomes normoblastic, the percentage of reticulocytes rises, and the haemoglobin content and erythrocyte and leucocyte counts of the circulating blood increase rapidly to values 3 or 4 times greater than before treatment.

L. Firman-Edwards

518. **Further Studies on Hemoglobin C—I. A Description of Three Additional Families Segregating for Hemoglobin C and Sickle Cell Hemoglobin**

J. V. Neel, E. Kaplan, and W. W. Zuelzer. *Blood* [*Blood*] **8**, 724–734, Aug., 1953. 2 figs., 7 refs.

The authors point out that it is possible to distinguish at least four genetically distinct types of haemolytic anaemia associated with the sickling phenomenon, which are due respectively to: (1) homozygosity for the sickle-cell gene; (2) the simultaneous presence of the sickle-cell

gene and the gene responsible for haemoglobin C; (3) the simultaneous presence of the sickle-cell and thalassaemia genes; and (4) the concurrence of the sickle-cell gene and of the gene responsible for haemoglobin D. In this paper are described three American negro families segregating for haemoglobin C and for sickle-cell haemoglobin. The data suggest that haemoglobin C is the result of the action of a single gene which appears to have a high degree of penetrance. There is no evidence of sex linkage. No conclusion can as yet be reached as to whether the sickle-cell and the haemoglobin-C genes are allelomorphs. *H. Lehmann*

519. **Further Studies on Hemoglobin C—II. The Hematologic Effects of Hemoglobin C Alone and in Combination with Sickle Cell Hemoglobin**
E. KAPLAN, W. W. ZUELZER, and J. V. NEEL. *Blood* [*Blood*] **8**, 735–746, Aug., 1953. 8 figs., 5 refs.

The authors have now studied, at the Children's Hospital (University of Michigan), Detroit, 7 cases of sickle-cell–haemoglobin-C disease, 4 of which were in members of the families described in the preceding paper [see Abstract 518], and have also examined 14 individuals with the asymptomatic haemoglobin-C trait. Compared with the commonest type of sickle-cell anaemia, that due to homozygosity for the sickle-cell gene, sickle-cell–haemoglobin-C disease is milder and causes less haemolysis. There are fewer sickled erythrocytes and siderocytes in blood smears, the most striking feature of which is the presence of target cells in large numbers. The resistance of the erythrocytes to hypotonic salt solutions is increased. Although the amount of haemolysis, as measured by the faecal urobilinogen excretion, is less than that seen in classic sickle-cell anaemia, the patient's erythrocytes, when transfused into normal recipients, are rapidly eliminated and have a half-life of only 10 days.

In individuals with the combination of haemoglobin C and normal haemoglobin the only significant morphological abnormality of the erythrocytes is the presence of numerous target cells, the frequency of which in the authors' cases varied from 3 to 33%. The condition is clearly differentiated from thalassaemia by the absence of microcytosis, hypochromasia, and abnormalities in the erythrocyte contour. Studies of erythrocyte survival in these cases gave contradictory results: although there was no evidence that increased haemolysis occurred in the donors, on a number of occasions the survival of the donor's cells was reduced on transfusion into normal recipients. *H. Lehmann*

520. **Filter Paper Electrophoresis of Human Hemoglobins with Special Reference to the Incidence and Clinical Significance of Hemoglobin C**
E. W. SMITH and C. L. CONLEY. *Bulletin of the Johns Hopkins Hospital* [*Bull. Johns Hopk. Hosp.*] **93**, 94–106, Aug., 1953. 4 figs., 21 refs.

A simple and inexpensive apparatus has been devised for the electrophoresis of hemoglobin solutions on filter paper. By the use of this device it is possible to recognize and separate hemoglobins A, S, C and F. The technique is well suited for application to mass surveys to determine the incidence of various abnormal hemoglobins. Such a survey has been conducted in the outpatient clinics of the Johns Hopkins Hospital. In a study of the hemoglobins of 500 white persons, no instance of S, C or D hemoglobin was discovered. However, in 500 negroes surveyed, hemoglobin S was found to occur in 8·4% and hemoglobin C in 2%. The combination of hemoglobin S and hemoglobin C in the same patient gives rise to a disease entity which on clinical grounds is readily differentiated from sickle cell anemia. Case histories of 7 such patients are presented. —[Authors' summary.]

521. **Familial Non-spherocytic Haemolytic Anaemia**
T. D. S. HOLLIDAY. *Journal of Clinical Pathology* [*J. clin. Path.*] **6**, 219–223, Aug., 1953. 3 figs., 15 refs.

In this paper are reported the clinical and haematological findings in 4 cases, seen at the West Cornwall Hospital, Penzance, of chronic haemolytic anaemia occurring in two generations of the same family; 5 other relatives were possibly also affected. The main features of the disease were its chronic course, a macrocytic blood picture, normal osmotic fragility, and basophilic stippling of the erythrocytes. Sickling could not be demonstrated. Erythrocyte survival studies carried out *in vitro* in one of the cases showed that the patient's erythrocytes underwent autohaemolysis more rapidly than normal erythrocytes when suspended in sterile saline solution: in plasma, on the other hand, their survival appeared to be abnormally prolonged. The author compares his cases with the few other reports in the literature of non-spherocytic haemolytic anaemia. The point is made that splenectomy is unlikely to be of value.

[The most interesting feature of this report is the demonstration of a raised rate of autohaemolysis in saline but not in plasma.] *J. V. Dacie*

HAEMAGGLUTINATION

522. **Hemolytic Disease of the Newborn Infant Caused by Maternal Sensitization to the Blood Factor hr′ (c). Report of Two Cases with Special Reference to the Etiologic Significance of Multiple Blood Transfusions in Rh Positive Women prior to Gestation**
J. GRUNDORFER. *Blood* [*Blood*] **8**, 609–619, July, 1953. 21 refs.

The author reports 2 cases of antibodies against the hr′ (c) blood factor occurring in the blood of Rh-positive white women of genotypes R_1R_1 (CDe/CDe) or R_1r' (CDe/Cde) investigated at Newark Beth Israel Hospital, New Jersey. Both women bore babies affected by haemolytic disease, one mildly and one severely, and both women had previously received blood transfusion. In one case the woman had been incorrectly typed as Rh negative and had consequently received Rh-negative blood. The rarity of this type of isoimmunization is illustrated by the following figures from the same laboratory. In a 5-year period, the blood of 12,226

pregnant women was examined, of whom 1,628 (13·98%) were found to be Rh negative. In addition 580 women known to be Rh negative were referred for other examinations. Evidence of isoimmunization against the Rh factor was found in 139 of these women, and 15 Rh-positive women showed evidence of ABO isoimmunization, whereas only 2 cases of hr′(c) isoimmunization occurred.

The discovery of antibodies against hr′ is discussed and the poor antigenicity of hr′ is noted. The importance of blood transfusion in stimulating the production of this particular antibody is stressed, attention being called to the possible danger of using Rh-negative blood for transfusion into Rh-positive women. *John Murray*

523. **Hemolytic Disease of the Newborn due to Anti-A**
H. CRAWFORD, M. CUTBUSH, and P. L. MOLLISON. *Blood* [*Blood*] **8**, 620–639, July, 1953. 4 figs., 28 refs.

A series of 11 cases of haemolytic disease of the newborn investigated at the Postgraduate Medical School of London is described in which the baby's blood was of Group A, that of the mother of Group O, and the only blood-group antibody found in the mother's serum was anti-A. In several other infants developing an unusual degree of jaundice after birth erythrocytes were found to be incompatible with maternal serum, although no evidence of excessive blood destruction was obtained; the difficulty of making a diagnosis in such cases is discussed. Groups of normal infants were also tested to establish the normal range of osmotic fragility of erythrocytes in the newborn, and also as a control for the observations on the 11 affected babies, while the osmotic fragility of the erythrocytes of 9 infants with haemolytic disease due to Rh antibodies was also determined for purposes of comparison.

Of the 11 mothers of affected babies, one had had no previous pregnancy, 2 had previously borne normal infants, and 2 had borne stillborn infants whose death was not apparently due to haemolytic disease. The remaining 6 had all previously borne infants with severe jaundice, and in 4 cases the diagnosis of haemolytic disease due to anti-A had been made at that time. Of the 4 specimens of cord blood tested, the haemoglobin concentration in 3 was below the normal range of 13·6 to 19·6 g. per 100 ml. In the remaining 7 cases venous blood was tested some hours after birth, when the haemoglobin concentration of 3 was below the normal range of 14·5 to 22·5 g. per 100 ml. All 11 babies had an increased reticulocyte count (between 8% and 21%) on the first day, and all blood films showed spherocytosis; in 7 cases out of 9 examined within 48 hours of birth there were 30 or more nucleated erythrocytes per 100 leucocytes. In contrast, spherocytosis was seen in the blood film in only one out of 6 of the control cases of haemolytic disease due to anti-Rh. The maximum plasma bilirubin concentration found in the 11 infants with haemolytic disease due to anti-A varied from 11 to 26 mg. per 100 ml. Osmotic fragility was above normal in 10 of these cases, whereas of the 9 infants with haemolytic disease due to anti-Rh, the osmotic fragility was considerably increased in 2, slightly increased in 2, and within the normal range in the remainder.

The survival of transfused erythrocytes of Groups A and O was studied in 2 cases in order to determine the severity, specificity, and length of action of the haemolytic process; during the following 6 days more than two-thirds of the Group-A cells were eliminated, whereas the Group-O cells survived normally. The direct antiglobulin (Coombs) test was weakly positive in 7 out of the 11 cases for a few days only. It was noticed in 2 cases that spontaneous clumping of the cells in freshly drawn blood occurred, and in one of these the phenomenon persisted for a fortnight; it was found incidentally and may well have been present in other cases. All 11 infants were secretors of A substance in the saliva. Only 2 of the mothers were Rh negative, neither having any anti-Rh in the serum, while in all 11 cases the mother's serum was able to haemolyse the baby's erythrocytes *in vitro*, the haemolysin titre for A_1 cells ranging from 6 to 120. The treatment given and the progress of the treated and untreated babies are described briefly.

Attention is drawn to the poor reactivity of A substance found in the erythrocytes of 26 normal babies, which were agglutinated much less strongly than adult cells with α_1 serum. *John Murray*

524. **The Syndrome of High-titre Cold Haemagglutination**
M. G. NELSON and R. J. MARSHALL. *British Medical Journal* [*Brit. med. J.*] **2**, 314–317, Aug. 8, 1953. 1 fig., 20 refs.

The authors describe 2 cases seen at the Royal Victoria Hospital, Belfast, in which, for no apparent reason, the serum contained cold agglutinins in high titre (1 in 20,480 at 0° C.). The patients, males aged 40 and 47, exhibited Raynaud's phenomenon when the hands were exposed to cold; one of them also had symmetrical dry gangrene of two digits, while the other was subject to attacks of haemoglobinuria when exposed to cold. Laboratory investigation revealed cold agglutinins in the serum of both patients. In addition signs of a chronic haemolytic anaemia were found in one patient; the other was only slightly anaemic. The reaction to the Coombs test was positive in both.

The authors conclude that the vascular signs and symptoms were due to intravascular autoagglutination brought about by cold, and that the gangrene was the result of thrombosis occurring after prolonged exposure to cold. They attribute the haemolytic phenomena to mechanical destruction of agglutinated erythrocytes. One of the patients received a short course of ACTH (100 mg. daily for 6 days) and subsequently 63 g. of urethane given over a period of 3 weeks, without benefit. Administration of peripheral vasodilator drugs was also without effect. The authors conclude that the only practical measure is the avoidance of exposure to cold.
J. V. Dacie

525. **A New Rare Human Blood-group Antigen (Wr^a)**
C. A. HOLMAN. *Lancet* [*Lancet*] **2**, 119–120, July 18, 1953. 1 fig., 5 refs.

Respiratory System

526. **Primary Tracheal Tumors in the Infant and Adult**
J. G. Gilbert, L. A. Mazzarella, and L. J. Feit. *Archives of Otolaryngology* [*Arch. Otolaryng.* (*Chicago*)] **58**, 1–9, July, 1953. 1 fig., 6 refs.

Tumours of the trachea are rare, and are even more rare in children than in adults. Of 564 primary tracheal tumours reported in the literature only 43 (7·9%) occurred in children. Further, in adults 49·1% of these tumours were malignant, as against 6·9% in children. Of the malignant tumours in adults 78·5% were carcinomatous, whereas all the malignant tumours in children—3 cases—were sarcomatous, and all, oddly enough, occurred in girls. The most common type of benign tumour in adults was some variety of osteochondroma, less common being papilloma and fibroma. In children, papilloma predominated, but fibroma and angioma have also been reported. In adults the lower third of the trachea is the most common site; from such information as is available, the most usual site in children appears to be the upper third.

Symptoms depend on the site of the tumour, the type of attachment, and the size of the tumour relative to the width of the trachea. In children a tracheal tumour causes bouts of brassy cough, dyspnoea, and respiratory difficulty, with supra- and infra-sternal retraction. The differential diagnosis is from laryngismus stridulus and papilloma or cyst of the larynx. In adults, tumour of the trachea may be mistaken for asthma, chronic bronchitis, or tracheitis. Lateral radiographs of the neck may be of help, but diagnosis is best established by endoscopy. Many benign tumours can be removed bronchoscopically, but it may in some cases be necessary to perform laryngofissure and split the cricoid as well as opening the trachea. Adenoma or mixed salivary tumours tend to recur, so removal must be thorough and the site should be treated by electrocoagulation. With the new methods of repair of the trachea now available the prognosis of malignant tracheal tumour has improved, but radical dissection of lymph nodes in the neck should not be omitted.

F. W. Watkyn-Thomas

527. **The Use of Streptokinase–Streptodornase in the Treatment of Thoracic Empyema**
J. J. Finnerty. *Surgery, Gynecology and Obstetrics* [*Surg. Gynec. Obstet.*] **97**, 220–232, Aug., 1953. 25 figs., 12 refs.

It is pointed out that in thoracic empyema administration of antibiotics and injection of streptococcal fibrolysins may result in sterilization and lung expansion when followed by repeated aspiration. The author, at the Bellevue Hospital (New York University), has devised a technique in which multiple thoracocenteses are avoided by the introduction of an intercostal drainage tube. Injections of 100,000 or 200,000 units of streptokinase and about a quarter that amount of streptodornase are given, and the tube is clamped for 8 to 16 hours, the injections being repeated once or twice at intervals of 48 hours.

This technique was used in 15 cases, in 7 of which there was an associated pneumonia but no broncho-pleural fistula. The tube was removed in 2 to 6 days in 6 cases, and in 5 weeks in the remaining case in which the empyema was chronic. In the other 8 cases a broncho-pleural fistula was present, and associated conditions included lung abscess and carcinoma. In 6 of these the fistula was closed and the empyema space obliterated in 4 to 18 days. Even where the fistula failed to close, surgery was nevertheless made easier by absorption of fibrin deposits and expansion of the lung.

This procedure is also advocated after resection of the lung but only in the early postoperative period when the bronchial sutures are intact.

S. F. Stephenson

528. **Emergency Thoracotomy for Massive Spontaneous Haemopneumothorax**
J. Borrie. *British Medical Journal* [*Brit. med. J.*] **2**, 16–18, July 4, 1953. 14 refs.

A review of the literature has shown that of the 90 reported cases of massive spontaneous haemopneumothorax, in 19 the patient died. The author, who is thoracic surgeon to the Otago Hospital Board, New Zealand, describes 3 further cases occurring in a ship steward, a stevedore, and a schoolboy, aged 21, 26, and 18 respectively. In one case the massive haemorrhage did not occur until several hours after the initial spontaneous pneumothorax. All 3 patients were successfully treated by thoracotomy after a preliminary period of resuscitation. At operation it was found in the first case that haemorrhage had occurred from a group of small, localized, emphysematous bullae. In the second case the haemorrhage arose from the parietal end of a torn string adhesion at the visceral end of which were several small bullae; the bleeding was controlled, the clot evacuated and the lung inflated by the anaesthetist. In the third case there had been haemorrhage into the pleural cavity, and haemorrhagic fibrinous material was found thickly deposited on the surface of the lung. Both the upper and lower lobes were successfully decorticated. In all 3 cases the convalescence was uneventful.

R. L. Hurt

529. **The Value of Penicillin and Sulphadiazine Used Separately and in Combination in 200 Cases of Pneumonia**
L. D. Erasmus. *South African Medical Journal* [*S. Afr. med. J.*] **27**, 733–737, Aug. 29, 1953. 11 refs.

A study of the effect of penicillin and sulphadiazine, alone and in combination, in the treatment of pneumonia is reported from the University of Pretoria. A total of 200 Bantu patients with pneumonia were divided into three groups, the groups being given penicillin, sulpha-

diazine, and penicillin combined with sulphadiazine respectively. Tests *in vitro* of the sensitivity of the bacteria isolated from the sputum in 82 cases showed that about a quarter of the organisms were resistant to penicillin or sulphadiazine. Nevertheless, no significant difference in the results of treatment as between the three groups was observed. The mean duration of pyrexia was longest (5·1 days) in the patients receiving penicillin and sulphadiazine combined; when, however, the duration of the illness before admission was included, the period of pyrexia in the patients receiving penicillin appeared to be equally long (9·3 days in the penicillin-treated group and 9·2 days in the combined-treatment group). Delayed resolution was observed in patients with malnutrition, jaundice, massive pneumonia, and in those who developed pleural effusion. In the penicillin-treated group a relationship was found between delayed resolution and insensitivity *in vitro* of the bacteria isolated from the sputum; a similar relationship was not demonstrated in the group receiving sulphadiazine.

The author concludes that there is no sound reason for combining penicillin with sulphadiazine in the treatment of pneumonia. [If the total duration of illness is taken as a criterion, the results in the sulphadiazine-treated patients appear to be better (total duration 8·2 days) than the results in patients given penicillin or the two drugs combined.] *J. G. Scadding*

530. **The Clinical Problem of Infected Cystic Disease of the Lung**

R. H. MEADE and R. A. RASMUSSEN. *Diseases of the Chest* [*Dis. Chest*] **24**, 205–218, Aug., 1953. 7 figs., 1 ref.

On the basis of a series of 26 cases seen during the last 5 years the authors describe the clinical and pathological picture of infected cystic disease of the lung and discuss some of the problems of diagnosis and treatment. The patient has usually been symptomless until infection occurs and gives rise to an acute pneumonitis. The fever responds to the usual treatment, but cough persists—often with sputum, and sometimes with haemoptysis—and acute attacks may recur. The chest radiograph shows a persistent shadow, sometimes with appearances suggestive of multiple cysts, but the appearances are not always specific. If a radiograph has been taken before the onset of infection, it has usually been accepted as normal, but on close scrutiny indistinct linear shadows may often be discerned. A bronchogram excludes bronchiectasis, the local bronchi failing to fill or being distorted, while bronchoscopy shows bronchitic changes only.

Pathologically, a whole lobe is usually involved in the congenital cystic process, the cysts (which may range in number from 3 or 4 to very many) containing mucus or pus and seldom communicating with the bronchi. The cysts are generally lined with columnar epithelium, sometimes ulcerated or granular and sometimes replaced by squamous cells. The wall is of inflamed fibrous tissue containing no muscle or glands. Insignificant until infected, the cysts then coalesce and the inflammation persists. In the differential diagnosis, tuberculosis must be excluded. Chronic suppurative pneumonia or a multilocular lung abscess can sometimes only be distinguished by examination of an operation specimen, while the possibility of carcinoma can be ruled out only at operation.

The most satisfactory treatment is by surgical resection of the affected area—which usually entails lobectomy or even pneumonectomy. In 9 of the authors' cases resection was carried out, with one death, and these 9 cases are described in detail. In 2 others exploratory thoracotomy showed the lung to be too extensively involved to permit of resection. *M. Meredith Brown*

531. **Pulmonary Function and Circulatory Dynamics in Artificial Pneumoperitoneum. II. Studies on Patients with Pneumoperitoneum as a Therapeutic Measure in Pulmonary Emphysema**

R. C. KORY, D. C. ROEHM, G. R. MENEELY, and R. A. GOODWIN. *Diseases of the Chest* [*Dis. Chest*] **23**, 608–620, June, 1953. 3 figs., 20 refs.

An investigation was carried out at the Thayer Veterans Administration Hospital and Vanderbilt University School of Medicine, Nashville, Tennessee, to determine the effect of pneumoperitoneum on cardiac and pulmonary function in 5 patients (mean age 58) with chronic emphysema, in 4 of whom it was severe. Estimations of pulmonary capacity and function, gas content of the arterial blood, and intracardiac and pulmonary arterial and "capillary" pressures were carried out before, and again one month or more after, the induction of pneumoperitoneum.

Although all 5 patients showed an increase of diaphragmatic movement, this increase was not necessarily related to clinical improvement. Three patients whose inspiratory capacity increased, with reductions in total capacity and residual air, were improved clinically by the pneumoperitoneum, whereas the 2 patients who did not show these changes were not improved. Arterial oxygen saturation rose appreciably in 4 of the patients, while in the 3 patients who were improved the content and tension of carbon dioxide in arterial blood fell. In all 5 cases the cardiac output was reduced after the induction of pneumoperitoneum; in one patient with cor pulmonale there was a fall in pulmonary arterial pressure, whereas in 2 others, whose pulmonary arterial pressure was normal initially, it was reduced with the pneumoperitoneum; both of these patients were clinically improved. The pulmonary "capillary", right ventricular, and right auricular pressures were unchanged. Peripheral resistance increased with the reduction in cardiac output.

The authors conclude that the primary effect of pneumoperitoneum in chronic emphysema is to increase the range of movement of the diaphragm, which in some cases improves the ventilatory capacity and breathing reserve, with consequent clinical improvement. The failure to improve in other cases, despite an increase in diaphragmatic movement, remains as yet unexplained. As the benefit, when obtained, may be considerable, it would be of real help if the factors responsible could be more clearly determined. *Paul B. Woolley*

Urogenital System

532. **Treatment of Hyperkalemia in Acute Renal Failure Using Exchange Resins**
H. C. KNOWLES and S. A. KAPLAN. *Archives of Internal Medicine* [*Arch. intern. Med.*] **92**, 189–194, Aug., 1953. 2 figs., 12 refs.

The authors report, from the University of Cincinnati College of Medicine, a study of 10 patients suffering from acute renal failure, of whom 4 were treated with the ammonium form of a carboxylic cation-exchange resin, 6 served as controls, and all 10 were given the same basic treatment.

Whereas the serum potassium levels of the controls rose progressively, those of the patients receiving the exchange resin showed a decrease. The urinary excretion of potassium was small and could not account for this fall. Stool analysis showed a large elimination of potassium by this route in one of the patients given resin. The resin, which was given in small, frequently repeated doses, apparently produced no untoward effects.

The authors consider that such a resin should be administered in cases of acute renal failure when the serum potassium level reaches 6 mEq. per litre and the urine volume is less than 500 ml. per day.

G. Loewi

MALE GENITALIA

533. **Bilateral Adrenalectomy for Prostatic Cancer**
P. L. SCARDINO, C. L. PRINCE, and T. A. MCGOLDRICK. *Journal of Urology* [*J. Urol.* (*Baltimore*)] **70**, 100–109, July, 1953. 3 figs., 23 refs.

The evidence in favour of bilateral adrenalectomy in the treatment of selected cases of metastatic carcinoma of the prostate which have not been controlled by other anti-androgenic methods is reviewed. The operation was performed on 3 patients, each of whom had undergone orchidectomy and received oestrogenic therapy (in addition to prostatectomy in one case), but had relapsed after varying periods. In every case there were demonstrable bone metastases, causing intolerable pain, and local extension of growth outside the prostatic capsule; none had symptoms of urinary obstruction. Acute adrenal insufficiency at the time of operation was controlled with cortisone, deoxycortone acetate, and phenylephrine, while for subsequent maintenance therapy cortisone, together with increased salt intake, proved adequate.

All 3 patients experienced relief of pain within 10 to 12 days of adrenalectomy. In one case the cessation of pain was complete and the patient has remained symptom-free for 9 months; in addition, there has been complete regression of the primary lesion, and the blood picture, which previously showed evidence of marked depression of haematopoiesis, has returned to normal. In the second case relief of pain was prompt but incomplete, though the primary lesion slowly regressed in size; death occurred from cardiac failure 4 months after operation. The third patient had some relief of pain for a brief period, but developed paraplegia from spinal metastases and died 4 months after adrenalectomy. In the case in which the most successful result was obtained the growth was a well differentiated adenocarcinoma (with metastases in both adrenal glands), whereas in the other 2 cases it was undifferentiated. The serum acid-phosphatase level was above normal in each case before operation, but decreased following adrenalectomy, a gradual rise occurring later to and above the pre-operative level in all 3. No demonstrable changes could be seen in the bony metastases after the operation.

It is concluded that "the striking and persistent improvement in one of the three cases is sufficient stimulus to warrant further investigation".

H. McComb

534. **Testicular Tumors. A Clinicopathological Study**
F. J. DIXON and R. A. MOORE. *Cancer* [*Cancer* (*N.Y.*)] **6**, 427–454, May, 1953. 29 figs., 20 refs.

The clinical and histological findings and the results of a follow-up study in approximately 1,000 cases of testicular tumour are analysed, the material being obtained from the records in the U.S. Armed Forces Institute of Pathology, Washington, D.C. (Two earlier papers (Friedman and Moore, *Milit. Surg.*, 1946, **99**, 573, and Moore, *J. Urol.*, 1951, **65**, 693) dealt with the histogenesis, morphology, and classification of the tumours in these same cases.)

[This paper is so concise and the mass of information is so well ordered and clearly presented that the abstracter can do no more than warmly recommend all clinicians, radiologists, pathologists, and biologists interested in this field to study the original.] *L. Michaelis*

KIDNEY AND URETER

535. **Effect of Nitrogen Mustard on Clinical Course of Glomerulonephritis**
D. S. BALDWIN, P. G. MCLEAN, H. CHASIS, and W. GOLDRING. *Archives of Internal Medicine* [*Arch. intern. Med.*] **92**, 162–167, Aug., 1953. 4 figs., 10 refs.

On the basis of the effect of nitrogen mustard on antigen–antibody reactions and the likelihood of such a reaction occurring in glomerulonephritis, this substance was administered, at Bellevue Hospital, New York, on 41 occasions to 10 patients with chronic diffuse glomerulonephritis. Significant decrease in proteinuria occurred in 22 cases, and diuresis in 21, but all except one patient relapsed subsequently. To each of 5 patients

with acute diffuse glomerulonephritis a single course of nitrogen mustard was given. In this group a significant reduction of proteinuria occurred in 2 patients, while there was diuresis in the 2 cases showing oedema.

The authors do not recommend [as indeed the results and the unpredictable course of the acute condition treated would not warrant] the routine use of nitrogen mustard in the treatment of glomerulonephritis.

G. Loewi

536. **Effects of Hydrazinophthalazine (" Apresoline ") on Blood Pressure and Renal Function in Children with Acute Nephritis**

W. W. McCrory and M. Rapoport. *Pediatrics* [*Pediatrics*] **12**, 29–37, July, 1953. 3 figs., 7 refs.

Hydrallazine (" apresoline ") has been shown to possess the unusual property of increasing renal blood flow while lowering systemic blood pressure. The drug was therefore used at the Children's Hospital, Philadelphia, for reduction of the hypertension in 5 children with acute nephritis and in 2 with chronic nephritis. It was found that one single parenteral dose of the drug (0·2 to 0·25 mg. per kg. body weight) was sufficient to lower the systolic and diastolic blood pressure within 20 minutes. This action was usually accompanied by tachycardia, which was present as long as the effect of the drug lasted—between 2 and 4 hours. Further oral administration in doses of 50 to 200 mg. per day, according to body weight, was effective in maintaining the fall in blood pressure throughout several days until recovery from the renal condition set in. The results in the 2 children with chronic nephritis were much less impressive.

The lowering of the blood pressure, however, was found to be associated with changes in the glomerular filtration rate and renal plasma flow, although these changes were not apparently related to the degree of systemic vasodilatation. The authors are doubtful whether this potent hypotensive agent should be used in patients with uncomplicated hypertension. Apart from the tachycardia and renal changes already mentioned there was evidence of depressed renal excretory function, which in addition to such untoward general reactions as vomiting, dizziness, and oliguria, combine to make the use of the drug undesirable and potentially dangerous. *L. H. Worth*

537. **Puncture Biopsy of the Kidney. A Report of 55 Cases.** (Biopsia renal por punción. Comunicación de 55 casos)

V. Pardo, C. F. Cárdenas, and C. Masó. *Revista clínica española* [*Rev. clín. esp.*] **49**, 379–382, June 30, 1953. 6 figs., 5 refs.

The authors, working at the University Hospital, Havana, obtained 55 suitable specimens from a total of 90 attempts at renal biopsy on 80 patients. They discuss the value of the procedure and its contraindications. The technique consists in inducing a retropneumoperitoneum with oxygen and then placing a fenestrated metallic plate over the right lumbar area; the position of this plate relative to the kidney is determined by radiography and a puncture point is chosen midway between the renal poles. Local analgesia with procaine is followed by a skin incision and the biopsy is taken with a Silverman trocar and cannula. The specimen removed is halved, one half being fixed in alcohol (for enzyme study), the other half in formol (for study of lipids). Complications consist of local pain, microscopic haematuria, and a transient fever, while around the kidney itself a haematoma may develop or the renal pelvis may be damaged.

The histological appearances of the normal kidney are described. In 2 cases of so-called nephrosis there was no fatty degeneration of the tubules, but the alkaline-phosphatase content was diminished. Of 14 cases of the Kimmelstiel–Wilson syndrome, all showed hyaline degeneration of the efferent glomerular artery. It is noted that the renal condition may be focal and a negative biopsy finding does not therefore rule it out. A case of diabetes insipidus showed no renal abnormality. Of 5 cases of lupus erythematosus, 3 showed the typical " wire-loop " appearances. The authors were able to make a diagnosis of pyelonephritis in 2 cases of obscure uraemia in which the histological appearances were normal.

It is concluded that the procedure is of most value in chronic renal diseases of obscure origin.

Paul B. Woolley

538. **Some Observations upon Absorption after Ureterosigmoidostomy**

C. D. Creevy. *Journal of Urology* [*J. Urol. (Baltimore)*] **70**, 196–202, Aug., 1953. 3 figs., 19 refs.

At the University Hospital, Minneapolis, observations on the absorption of salts, especially urinary chlorides, from the colon were made on 5 patients who had undergone ureterosigmoidostomy, and the data in another case were examined. Absorption of chlorides from the bowel producing hyperchloraemic acidosis was a common finding after operation. It could be corrected by a low-salt diet and the administration of alkalis, or by unilateral nephrostomy, or by the continuous irrigation of the rectum with tap-water. Four factors influencing the development of hyperchloraemic acidosis have been suggested. These are: (1) the large surface area of the colon exposed to the urine; (2) the frequency and completeness of the evacuation of the urine; (3) the particular segment of the colon bathed by the urine; and (4) the state of the renal function. From his observations the author concludes that the most important factor is the state of the kidneys. The records of another 111 patients who had undergone ureterosigmoidostomy were examined and further evidence to support this contention was found.

After ureterosigmoidostomy the kidneys frequently undergo dilatation and infection, and it has been noted that hyperchloraemic acidosis is commoner and more severe in cases in which the renal function is demonstrably impaired. To prevent this development a terminal colostomy above the anastomosis is recommended. *W. Skyrme Rees*

See also Pathology, Abstract 363

Endocrinology

THYROID GLAND

539. **Evaluation of a Thyroid Panel. Practical Application of Scintillation Counter in Diagnosis of Diseases of the Thyroid**

T. F. Barrett, H. Peck, F. K. Bauer, R. L. Libby, and S. R. Jarrett. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **152**, 1414–1417, Aug. 8, 1953. 4 refs.

The authors set out to assess the value of determination of the uptake of radioactive iodine (^{131}I) by the thyroid gland in the diagnosis of thyroid disorders. In a pilot study carried out at the Veterans Administration Center, Los Angeles, on 116 healthy subjects and 213 patients with a variety of diseases, 2 μc. of carrier-free ^{131}I was administered in a capsule with a little tap-water after a light breakfast to each subject. A scintillation counter was used to measure the uptake at 6 and 24 hours later, background counts being obtained over the knee and subtracted from the count over the thyroid. Either on the same day or the day after, determinations were made of the basal metabolic rate (B.M.R.) and serum protein-bound iodine and cholesterol levels. Uptake values in the control group fell within the limits generally accepted, whereas of 273 tests performed on the 213 patients, 78 gave an abnormal result. Of the 17 patients whose uptake was abnormally high, all were suffering from hyperthyroidism except for one man with hypertensive cardiac failure whose uptake of ^{131}I at 6 hours was normal; his serum protein-bound iodine level was also normal, but his serum cholesterol level was raised. Of the 61 patients with a low uptake, only 19 were suffering from myxoedema or hypothyroidism due to ^{131}I therapy, thyroidectomy, or thyroiditis. Of the remaining low results, 28 were considered to be due to thyroid or iodine medication in one form or another, one to bromide intoxication, 3 to cortisone therapy, and 8 to the presence of a non-toxic thyroid adenoma; 3 were unexplained. Some patients who were noted as having values in the lower range of normal had recently undergone an operation, and the possibility of surgical trauma, as a form of stress, being the cause of this finding is mentioned tentatively. Normal figures were obtained in a case of carcinoma of the thyroid gland and in 5 patients whose thyroiditis had subsided.

The advantages of the tracer test over other tests of thyroid function are discussed. In cases of unequivocal hyper- or hypo-thyroidism determination of the B.M.R. gives results comparable with those of the tracer test, but its value is limited by the wide variation in results among normal subjects and its inability to detect hyperthyroidism in the absence of hypermetabolism. The serum cholesterol level is of assistance only in relation to hypothyroid states. However, the results of serum protein-bound iodine determinations are closely correlated with those of the tracer test in most instances; and the authors regard the combination of these two tests as " probably the best available laboratory tool for confirmation of the clinical impression of thyroid disease ". *R. St. J. Buxton*

540. **Relationship of the Age of the Patient to the Natural History and Prognosis of Carcinoma of the Thyroid**

G. Crile and J. B. Hazard. *Annals of Surgery* [*Ann. Surg.*] **138**, 33–38, July, 1953. 4 refs.

This paper is based on the study of 105 cases of carcinoma of the thyroid gland treated at the Cleveland Clinic, Cleveland, Ohio. Carcinoma of the thyroid is classified as papillary or non-papillary, the characteristics of the former being a slow rate of growth, absent or markedly delayed distant metastasis but early metastasis to the regional lymph nodes, infrequent invasion of blood vessels, and a tendency to occur in young adults and children. The malignant non-papillary tumours on the other hand grow rapidly and tend to invade the perithyroid tissues and blood vessels, giving rise to early distant metastases; they occur more commonly in older patients.

The authors state that " one of the most important and most neglected prognostic features of a cancer of the thyroid is the age at which it occurs. In patients under 40 years of age, any cancer of the thyroid is almost certain to be of a relatively low order of malignancy and, regardless of how little papillary configuration it shows, there is about a 95% chance that its clinical behaviour will be that of a papillary tumor. Conversely, if the patient is over 60 years of age and the tumor is not a clear cut papillary carcinoma, it is nearly always a highly malignant cancer with a very poor prognosis." The age of the patient is thus of much greater prognostic significance than the histological pattern of the tumour, and the outlook for the younger patient is almost universally good, provided that an adequate operation is performed. *N. Alders*

541. **Adenolipomatosis of the Thyroid. A New Type of Goiter**

V. E. Chesky, W. C. Dreese, and C. A. Hellwig. *Surgery* [*Surgery*] **34**, 38–45, July, 1953. 6 figs., 12 refs.

A rare form of goitre, termed adenolipomatosis of the thyroid, which was observed in a 15-year-old boy at the Hertzler Clinic, Halstead, Kansas, is described. There was a history of a lump in the neck, present since birth, which had gradually increased in size and had been regarded as a cystadenoma of the right lateral lobe of the thyroid gland. There was no thyrotoxicosis. At operation the tumour was found to be yellow and soft, con-

sisting mostly of fat in association with small masses of thyroid tissue. Histological examination of this tissue showed that the epithelium was cuboid and that the colloid was well stained; in other parts the tissue resembled embryonic thyroid. It was estimated that one-half of the right and four-fifths of the left lobe of the thyroid gland consisted of fat.

[Usually there is little if any fat in the normal thyroid, and this case must be regarded as a rare example of fatty replacement, such as is occasionally found in the kidney, uterus, beneath the pia of the spinal cord, or elsewhere in the central nervous system—for example, in the region of the corpus callosum. The precise nature and the origin of the fat in these cases are still obscure.]

Lambert Rogers

542. **The Treatment of Thyrotoxicosis with Radioactive Iodine.** (Traitement de la maladie de Basedow par l'iode radioactif)

—. GILBERT-DREYFUS, —. AMBROSINO, —. ZARA, and —. TRIANTAPHYLLIDIS. *Presse médicale* [*Presse méd.*] **61**, 941–943, June 27, 1953. 4 figs.

The authors have treated, at the Hôpital de la Pitié, Paris, 100 cases of thyrotoxicosis with radioactive iodine (^{131}I), and 62 of these cases have been observed for at least 8 months after treatment. The indications for treatment were those commonly accepted, and the dose administered depended on the effective life of the radioactive iodine in the thyroid gland, this being determined by a preliminary tracer experiment in each patient. A number of other factors influenced the dose required; for example, larger doses were required in severe cases, when the gland was very large, and for young patients; toxic adenoma was particularly resistant. Smaller doses were found to be adequate in milder cases and for older patients.

In assessing the results of treatment, the authors differentiate between " apparent cure ", that is, when the patient became euthyroid clinically but the thyroid radioactive-iodine fixation curve remained abnormal, and " total cure ", in which both the clinical findings and radioactive-iodine fixation curve were normal. In the 23 patients who appeared euthyroid clinically but in whom the thyroid curve remained abnormal there was often a recurrence of the disease in the ensuing months, requiring further treatment with radioactive iodine. Of the others, 23 were completely cured, in 13 the improvement was considered insufficient, and 3 did not complete the course for various reasons. *G. Ansell*

543. **The Effect of L-3 : 5 : 3′-Triiodothyronine in 10 Cases of Thyroid Insufficiency.** (Effet de la L-3, 5, 3′- triiodothyronine sur dix cas d'insuffisance thyroïdienne)

L. DE GENNES, G. DELTOUR, and J. LEPRAT. *Presse médicale* [*Presse méd.*] **61**, 1119–1121, Aug. 29, 1953. 7 figs., 18 refs.

Since the first reports on the use of L-triiodothyronine in 1952 some doubt has persisted about its activity relative to that of thyroxine, owing partly, it is thought, to differences in the methods of comparison. In the present study, carried out at the Faculty of Medicine, Paris, 10 cases of thyroid insufficiency were treated with an intramuscular dose, usually of 0·1 mg. per day, of the hormone for periods of 5 to 23 days. Excellent results were obtained in 5 cases, intolerance occurred in 2 patients, both of whom had previously shown intolerance to L-thyroxine, and results were mediocre in the remaining 3, of which 2 were cases of myxoedema of pituitary origin. These results suggest that this hormone is equally active when given intramuscularly as in the same dose by mouth, and that it is more active against all the signs of hypothyroidism than any other mode of administration of thyroxine. *C. L. Cope*

544. **The Use of Thyrotrophin in the Differential Diagnosis of Primary and Secondary Hypothyroidism.** [In English]

B. SKANSE. *Acta endocrinologica* [*Acta endocr.* (*Kbh.*)] **13**, 358–370, Aug., 1953. 1 fig., 11 refs.

Certain cases of myxoedema do not respond well to treatment with thyroid, and it has been shown that the condition in these patients is part of a more generalized disturbance due primarily to failure of the anterior pituitary. The differentiation between this secondary type of myxoedema and primary hypothyroidism is usually easy, but may in certain instances be extremely difficult; a test based on measurement of the response of the thyroid gland to thyrotrophic hormone has therefore been suggested as an aid to diagnosis, and the author here reports his experience with such a test.

The response to thyrotrophic hormone was studied in 10 euthyroid persons, 10 patients with typical primary thyroid myxoedema, and 8 patients with definite evidence of hypopituitarism together with myxoedema. The thyrotrophic hormone was administered intramuscularly in daily doses of 20 units for 6 days or longer. Before and after treatment with the hormone the thyroid function was assessed from: (1) the serum protein-bound iodine level; (2) the basal metabolic rate; (3) the 48-hour urinary excretion of radioactive iodine (^{131}I); and (4) the " extrarenal disposal rate " of ^{131}I (that is, the rate at which ^{131}I is removed from the blood by all tissues other than the kidneys, principally by the thyroid gland). The dose of ^{131}I used was 10 to 50 μc., with 100 μg. of ^{127}I as carrier.

In the euthyroid patients the administration of thyrotrophic hormone produced marked signs of stimulation of the thyroid gland. No corresponding evidence of stimulation occurred in any of the patients with primary thyroid myxoedema, whereas in the patients with pituitary myxoedema there were signs of thyroid hyperfunction after treatment with the hormone, although the response was not quite so evident as in the normal subjects.

These results indicate that determination of the response to thyrotrophic hormone may be useful in the differential diagnosis between primary and secondary hypothyroidism, and possibly also in detecting mild degrees of hypothyroidism. However, more experience, especially in this last type of case, is necessary before the value of the method can be finally judged.

Nancy Gough

ADRENAL GLANDS

545. **The Thymus Involution Test for ACTH.** [In English]
E. THING. *Acta endocrinologica* [*Acta endocr.* (*Kbh.*)] **13**, 343–352, Aug., 1953. 4 figs., 7 refs.

The usual method used for the assay of ACTH (corticotrophin), the ascorbic acid depletion test, suffers from the disadvantage that it requires hypophysectomized animals. A method involving the use of intact animals, based on an observation by Hayashida and Li (*Endocrinology*, 1952, **50**, 187) that the weight of the thymus decreases under the influence of ACTH in normal 21-day-old rats, has been described by Bruce *et al.* (*Lancet*, 1952, **1**, 790), and has been further investigated by the present author, 1,500 nestling rats 7 to 10 days old being used. Since the thymus requires a constant stimulus, the ACTH was administered in an oily medium consisting of arachis oil with 5% beeswax. Injections were given once daily for 3 days, and 24 hours later the thymus was removed and weighed. From the average results obtained with different doses, dose–response curves were constructed. The oily medium alone was without effect on the thymus, and stress substances such as formalin had to be administered in very large amounts before more than slight involution occurred, whereas it was confirmed that a quantitative relation existed between the dose of ACTH administered and the degree of thymus involution produced. The reliability of the test seemed to be equal to that of established methods, but its sensitivity was less, the amount of active material necessary to produce a significant response being about 10 times greater than in the ascorbic acid depletion test.

Nancy Gough

546. **The Enhancement of the Effect of ACTH on the Adrenal Weight and the Thymus Involution in Hypophysectomized Rats when Administered in Beeswax–Oil.** [In English]
E. THING. *Acta endocrinologica* [*Acta endocr.* (*Kbh.*)] **13**, 353–357, Aug., 1953. 2 figs., 12 refs.

Concurrently with the work reported in the preceding paper [see Abstract 545], the author administered ACTH (corticotrophin) in oil–beeswax suspension to adult hypophysectomized rats and investigated its ability to produce adrenal hypertrophy and thymus involution. The study was begun 14 days after hypophysectomy and the 155 rats were divided into three groups, the first being given ACTH in aqueous solution, the second ACTH in arachis oil with 5% of beeswax, and the third being used as controls. The ACTH was given at various dosage levels (5 animals per dose), the doses given in aqueous solution being ten times greater than those given in oily suspension. The degrees of thymus involution and adrenal hypertrophy found after 3 days' treatment were about equal in both groups, indicating that one dose of the slowly-absorbed ACTH preparation is equal in effect to 10 doses of aqueous ACTH. Nevertheless, the amount of hormone required to obtain a measurable response was ten times greater than that required when intact nestling rats were used, and the author therefore concludes that the method of assay of ACTH by determination of its effect on the adrenal weight and thymus involution in adult hypophysectomized rats is of no practical value.

Nancy Gough

547. **Correlation of the Eosinophil Count with the Clinical Course during Cortisone and ACTH Therapy**
J. R. MARTIN and C. J. PATTEE. *Canadian Medical Association Journal* [*Canad. med. Ass. J.*] **68**, 565–569, June, 1953. 25 refs.

The relationship, if any, between a rise or fall in the eosinophil count and the clinical changes in patients receiving cortisone or ACTH was studied at Queen Mary Veterans' Hospital, Montreal. In 35 of 56 patients, most of whom were suffering from bronchial asthma or rheumatoid arthritis, there was a fall in the eosinophil count of at least 50% after administration of cortisone, but no parallel was observed between this fall and the efficacy of the treatment. In 20 of these 35 patients the eosinophil count rose later during treatment (" escape " of eosinophils), but again there was no apparent association with any alteration in the clinical condition. In the authors' view ACTH is a stronger eosinopenic agent than cortisone [this view, however, is based on the results in only 2 cases, in which a course of ACTH was given after a course of cortisone]. They state that if two courses of cortisone are given, the fall in the eosinophil count is less during the second course [but this finding is based on 3 cases only, in one of which the second course was given after an interval of one year]. The authors found wide variations in the eosinophil count in the same patient, even when it was determined at the same time each day. [These variations, which have been noted by many other workers, do not prevent them from formulating theories based on this wide scatter.]

H. Herxheimer

548. **Cortisone and the Metabolic Response to Injury**
R. M. CAMPBELL, G. SHARP, A. W. BOYNE, and D. P. CUTHBERTSON. *Nature* [*Nature* (*Lond.*)] **172**, 158–160, July 25, 1953. 1 fig., 21 refs.

It has been observed that the increased protein catabolism following injury such as fracture strikingly resembles the effect of the administration of ACTH (corticotrophin) or cortisone. In the present investigation, carried out at the Rowett Research Institute, Aberdeen, the results in these two events were compared, using rats as the experimental subjects. Male rats weighing 300 g. and maintained on a constant food intake were divided into 4 groups of 6 animals each and treated in one of the following ways: (1) subcutaneous implantation of 25 mg. of cortisone acetate; (2) fracture of the femur by open operation; (3) subcutaneous implantation of 50 mg. of cortisone acetate; or (4) fracture of femur plus implantation of 25 mg. of cortisone acetate subcutaneously. A control group was treated by sham operation and showed little disturbance of nitrogen metabolism.

Estimation of the urinary nitrogen output in the test

animals showed that the effect of fracture was similar in character and magnitude to that of implanting a 25-mg. pellet of cortisone acetate. The result of adding a second 25-mg. pellet through the same incision was similar to that of simultaneous fracture and implantation of one pellet; in both cases the effect was greater than for one event only, but not as great as if they were additive. These observations suggest that the effect of fracture of the femur in the rat is roughly equivalent to the effect of the slow liberation of 25 mg. of cortisone from the adrenal cortex, and that increasing the stimulus (as measured by cortisone) increases the response. It is not considered justifiable at present, however, to conclude from this that any such injury would cause the liberation of such a quantity of glucocorticoid from the adrenal cortex. *Nancy Gough*

549. **Postoperative Adrenal Cortical Insufficiency. Occurrence in Patients Previously Treated with Cortisone** R. M. SALASSA, W. A. BENNETT, F. R. KEATING, and R. G. SPRAGUE. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **152**, 1509–1515, Aug. 15, 1953. 5 figs.

In this paper from the Mayo Clinic 2 cases are described in which, following prolonged administration of cortisone for rheumatoid arthritis, the patients died from irreversible shock after a major surgical operation.

The first patient, a woman of 54 years, had received cortisone for one year before admission in a dosage of 75 mg. 3 times a week, increased after 4 months to 100 mg. a day. Symptoms of gastric ulceration developed and 7 days after admission a haematemesis occurred. A partial gastrectomy was performed, but the patient did not regain full consciousness; signs of shock developed and she died despite emergency measures which included the administration of 300 mg. of cortisone.

The second patient, also a woman of 54 years, had received a prolonged course of both cortisone and ACTH for rheumatoid arthritis. During this treatment she developed moon-face. Administration of cortisone was discontinued when the patient was admitted to hospital for treatment of the rheumatoid arthritis, but intra-arterial injections of hydrocortisone to a total of 422 mg. were given in the 4½ months before bilateral bunionectomy was performed, the last injection being given 2 weeks before the operation. The patient withstood the operation well, but 15 hours afterwards shock developed which did not respond to cortisone and intravenous injection of hydrocortisone.

In both patients the basophilic cells of the anterior pituitary showed loss of granulation, vacuolization, and hyalinization, while the adrenal cortex was considerably decreased in thickness, owing to a diminished number of cells rather than to diminished cellular size. There was lack of lipoid material in the zona glomerulosa and zona fasciculata, with congestion of the zona reticularis.

The authors also examined the adrenal glands of adult patients who had died from various disease conditions for which they had received cortisone. It was found that there was often a decrease in the size of the glands, that even when the total adrenal weight was normal there were often marked histological changes, and that when cortisone treatment had been discontinued several weeks or months before, signs of recovery were apparent. It is pointed out that these changes are due to reduced endogenous production of ACTH, and that the same situation, with the same hazards, might arise after prolonged treatment with this hormone.

In the authors' view, a patient who has received intensive ACTH or cortisone therapy within a period of 6 to 12 months before operation, particularly if there are signs of hypercorticism, should be regarded as having deficient reserve adrenocortical function. Intramuscular injections of 200 mg. of cortisone should be given 48, 24, and 1 to 2 hours before operation, with a gradual tailing off of the drug during the subsequent 3 to 4 days. The patient should not receive intravenous infusions of glucose solution without sodium chloride, and morphine, which is also dangerous to patients with deficient adrenocortical function, should be avoided. *G. A. Smart*

550. **Pre- and Postoperative Care in Adrenal Surgery** J. W. JAILER. *Journal of Urology* [*J. Urol.* (*Baltimore*)] **70**, 137–140, Aug., 1953.

Only since the introduction of cortisone has radical adrenal surgery become reasonably safe. The different steroids of the adrenal cortex have markedly different physiological effects, and these are discussed in detail. It is not yet known which steroids the human adrenal cortex secretes, but Compound F (17-hydroxycorticosterone) may be one of them.

Total adrenalectomy may be carried out for malignant hypertension, or prostatic or mammary carcinoma. If performed in two stages no special preparation is necessary for the first stage. For the second stage, or when a one-stage operation is performed, 200 mg. of cortisone is given intramuscularly the day before. On the day of operation this dose is repeated together with 5 mg. of deoxycortone acetate (DCA). This treatment is repeated on the first postoperative day and then the cortisone is tapered off to a maintenance dose of between 12·5 and 50 mg. daily.

It has not been established whether Cushing's syndrome is primarily due to the formation of too much Compound F by the adrenal cortex or too much ACTH by the pituitary gland. The clinical manifestations of the disease are due to excessive adrenal cortical secretion. The removal of the source of these steroids is the rational approach to therapy. Cushing's syndrome may also be caused by carcinoma or benign adenoma in the cortex. When a tumour exists in Cushing's syndrome the contralateral gland is invariably atrophic, so that without hormonal preparation removal of one adrenal may result in the patient becoming fully adrenalectomized, a condition which is incompatible with life. Cortisone and DCA must be given for immediate replacement, together with ACTH to stimulate the function of the atrophic gland. The blood pressure must be maintained in the immediate postoperative period and the sodium and potassium levels corrected if necessary.

The androgenital syndrome (adrenal virilism) may be due to adrenal hyperplasia or neoplasm. Owing to

differences in the steroids elaborated by the adrenal in this condition as compared with Cushing's syndrome the metabolic changes in the two conditions are not at all similar and operation presents quite different problems. These patients stand surgery very well and healing is prompt with little or no hormonal support. The mixed syndrome showing both androgenic and Cushing features should be handled as for a Cushing syndrome when it is due to adrenal carcinoma. When due to benign adenoma no hormonal support is necessary. In patients with adrenal virilism due to bilateral adrenal hyperplasia the administration of cortisone results in decrease of adrenal secretion by inhibition of ACTH. On the other hand, when carcinoma is present cortisone is without effect—evidence that adrenal carcinoma is independent of pituitary stimulation.

W. Skyrme Rees

551. **Surgery of the Adrenal Gland for Cushing's Syndrome**

E. F. POUTASSE and C. C. HIGGINS. *Journal of Urology* [*J. Urol.* (*Baltimore*)] **70**, 129–136, Aug., 1953. 6 figs., 11 refs.

It is now generally accepted that all patients with Cushing's syndrome have hyperadrenocorticism, with excess of 11-oxysteroids. In some cases the condition is due to a tumour of the adrenal gland, but more often to hyperfunction of the adrenal cortex, with or without hyperplasia. The stimulus causing the hyperadrenocorticism is not understood and it is only rarely that a basophilic pituitary tumour can be demonstrated. The excess of 11-oxysteroids produces the characteristic signs of Cushing's syndrome. If there is excess of steroid metabolites resembling androgens, the androgenic syndrome and Cushing's syndrome may be found in the same individual. Cushing's syndrome is twice as common in women as in men. The average age of onset is 30, and the span of life is shortened, although occasionally spontaneous remission does occur.

In this paper the results of treatment of 28 cases of Cushing's syndrome are presented from the Cleveland Clinic, Ohio. Of these, 2 were found to have a malignant tumour of the adrenal cortex, 4 a benign solitary adenoma of the adrenal gland, in 2 cases solitary benign adenomata occurred in hyperplastic glands, and in the remaining 20 cases no tumour was found. Methods of diagnosis are discussed. Treatment consists in either excision of any existing tumour or subtotal adrenalectomy, in which all of one adrenal gland and 90% of the other is removed at a one-stage operation. At present it is not considered necessary to perform bilateral total adrenalectomy unless the disease is progressive following subtotal adrenalectomy and presents a threat to life. Simultaneous bilateral inspection of the adrenals is advised before any definitive operative procedure on the glands is performed. If both glands appear atrophic, search must be made for a cortical adenoma in an aberrant situation, accessory adrenal tissue being present in 20% of all individuals.

The use of cortisone and other hormones in replacement therapy is discussed. Operation has been made safer by the preoperative administration of cortisone, which is continued in decreasing doses after operation, or it may have to be continued indefinitely if the remaining adrenal fragment is incompetent. ACTH may be used in order to stimulate an atrophic gland, and deoxycortone acetate may also be necessary after operation. With adequate resection of the adrenals almost all the abnormal features disappear, although osteoporosis, which is often present, is late in responding. Hypertension, possibly due to irreversible changes in the arteries, is sometimes uninfluenced by operation, and serious vascular disease may occur at an early age in Cushing's syndrome in spite of adequate therapy.

In a group of 8 patients operated on since cortisone became available there were no operation deaths. One died 9 months after operation from perforated duodenal ulcer, another required a second operation for total adrenalectomy, but the other 6 are well. Of an earlier group of 12 patients, one died; of 5 subjected to bilateral hemi-adrenalectomy, 3 are well, one is improved, and one died of adrenal failure. Finally, of 5 patients who underwent exploration only, the 3 who were traced all died of complications of Cushing's syndrome.

W. Skyrme Rees

552. **Comparative Study of the Use of Glycyrrhizinic and Glycyrrhetinic Acids in Addison's Disease**

H. E. PELSER, A. F. WILLEBRANDS, M. FRENKEL, R. M. VAN DER HEIDE, and J. GROEN. *Metabolism* [*Metabolism*] **2**, 322–334, July, 1953. 9 figs., 11 refs.

Two of the active principles of liquorice, which has itself been shown to maintain electrolyte equilibrium in patients with Addison's disease, were investigated at the Wilhelmina Hospital, Amsterdam.

Glycyrrhizinic acid is a combination of glucuronic (glycuronic) acid and a triterpene called glycyrrhetinic acid. The authors describe 3 cases of Addison's disease in which the electrolyte balance was determined during administration of glycyrrhizinic and glycyrrhetinic acids by mouth. It was found that either of these substances in a dose of approximately 5 g. a day rapidly corrected the abnormal electrolyte state, glycyrrhetinic acid being the more powerful of the two. It is concluded that liquorice or its active constituents can be used successfully in the treatment of Addison's disease.

G. S. Crockett

553. **Further Experience in the Treatment of Addison's Disease with Extract of Liquorice and Glycyrrhetinic Acid.** (Verdere ervaringen over de behandeling van de ziekte van Addison met succus liquiritiae en glycyrrhetinezuur)

H. E. PELSER, A. F. WILLEBRANDS, and J. GROEN. *Nederlandsch tijdschrift voor geneeskunde* [*Ned. T. Geneesk.*] **97**, 1900–1905, July 18, 1953. 3 figs., 9 refs.

The daily oral administration of 5 to 30 g. of liquorice extract or 0·25 to 2·5 g. of glycyrrhetinic acid, which would appear to contain a substance causing retention of sodium and chloride and increased excretion of potassium, was sufficient to maintain 4 patients suffering from Addison's disease at the Wilhelmina Hospital, Amsterdam, in electrolyte balance and in excellent con-

dition for periods of 1 to 2½ years; 2 of the patients got over concomitant infections without difficulty. Continued use of these drugs appeared to produce increased sensitivity to them, and in all cases the dose adequate to maintain electrolyte equilibrium could, after periods of weeks or months, be considerably reduced, in 2 cases to one-tenth of the original dose.

The effects of excessive dosage became manifest in headache, shortness of breath, oedema with or without raised blood pressure, and later hypertension unaccompanied by oedema. The similarity of the sequence (in which the urine showed no abnormality) to that seen in the development of chronic from acute nephritis suggests that a similar mechanism to that producing hypertension in nephritis lies behind the phenomena of overdosage. Brief clinical records of the 4 cases are given. *R. Crawford*

PANCREAS

554. **Insulin as a Growth Hormone**
J. SALTER and C. H. BEST. *British Medical Journal* [*Brit. med. J.*] **2**, 353–356, Aug. 15, 1953. 5 figs., 13 refs.

The great sensitivity of the hypophysectomized animal to insulin has hitherto prevented the successful investigation of the effect of this hormone on the growth of the animals. The present authors, at the University of Toronto, have been able to stimulate rapid growth in completely hypophysectomized rats by one daily injection of protamine zinc insulin (P.Z.I.).

The results of 3 experiments are reported. In Experiment A, 40 male hypophysectomized rats were divided into 3 groups: the first group were killed on the first day to secure basal levels; the second group received P.Z.I. daily for 15 days; the third received no insulin and were killed at the same time as the insulin-treated animals. An average gain in weight of 38 g. (in 15 days) was observed in the insulin-treated animals and necropsy revealed an absolute increase in the weight of thymus, kidney, heart, and liver. There was a definite increase in body protein, but the body fat was increased to a greater extent than either protein or water. The tibia test of Greenspan *et al.* (*Endocrinology*, 1949, **45**, 455) showed definite evidence of skeletal growth.

In Experiment B another 40 rats were divided into three groups: the first received one dose of P.Z.I.; the second received a dose of growth hormone each day for 15 days which was regulated to produce a rate of growth similar to that in the insulin-treated animals in Experiment A; the third group, which served as controls, received the same diet as the other two groups. Necropsy showed that the insulin-treated animals stored more fat and less water than those treated with growth hormone, although the average gain in weight and final weight were the same in both groups.

In Experiment C, 53 hypophysectomized rats were divided into a control group, a group treated with growth hormone, and a group treated with P.Z.I. The increase in weight of both insulin- and hormone-treated animals was 42 g. in 15 days, the dosage of both substances being approximately the same as in Experiment B. The average increase in protein was greater in the hormone-treated (4·0 g.) than in the insulin-treated group (2·6 g.); similarly, the increase in width of the epiphysial disk was 154 μ in the hormone-treated group and 75 μ in the insulin-treated group.

Discussing their findings, the authors suggest that under physiological conditions insulin works synergistically with the somatotropic factor of the anterior pituitary and with other hormones which, in the complete absence of insulin, exert predominantly catabolic effects. Considering the clinical significance of their demonstration that insulin causes rapid growth in the hypophysectomized animal, they recall that while there is no direct evidence that somatotropin causes any liberation of insulin, it does cause an increase in pancreatic islet-cell volume. The possibility that a failure of adequate insulin liberation may be one of the many factors limiting growth in the human pituitary dwarf is suggested. *J. Lister*

555. **Mechanism of Lowered Renal Threshold for Glucose in Diabetes**
J. A. ROBERTSON and C. H. GRAY. *Lancet* [*Lancet*] **2**, 12–15, July 4, 1953. 4 figs., 10 refs.

When the load of glucose presented to the renal tubules by glomerular filtration is greater than the rate at which glucose can be absorbed, glycosuria occurs. This load is the product of glucose concentration in the glomerular filtrate and the glomerular filtration rate. The authors, at King's College Hospital, London, have studied the mechanism of glucose absorption in 12 diabetic patients (4 men and 8 women, of whom 3 were pregnant) who exhibited a lowered renal threshold for glucose. None of the patients had evidence of impaired renal function as shown by the usual laboratory tests. A further 6 patients with severe diabetes but with normal renal threshold for glucose were used as controls. The thresholds in all the cases were determined 4 hours after the morning dose of insulin; the patient emptied his bladder, 10 minutes later the blood sugar level was estimated, and immediately afterwards the bladder was again emptied. Glomerular filtration rate was measured by inulin clearance, the effective renal plasma flow by the *p*-aminohippurate clearance, and tubular reabsorption of glucose at rising plasma glucose levels by the method of Robertson *et al.* (*Arch. intern. Med.*, 1951, **87**, 570). The glucose tubular absorption was measured, at 3 plasma glucose levels after infusion of glucose, by the method of Schaffer and Hartman (*J. biol. Chem.*, 1921, **45**, 365).

In 3 cases high glomerular filtration rates were found, and in one of these the renal plasma flow was above normal, a finding which the authors explain by the fact that the patient was very small and the correction factor for standard surface area very large. In 6 cases glucose reabsorption was determined at only one plasma glucose level, which in each was above that at which maximum reabsorption was expected; in all these cases the values for tubular reabsorptive capacity were above the normal range. In the other 6 patients more than one estimation was made. At low plasma glucose levels,

glycosuria was present, suggesting that reabsorption was less than normal. (It was assumed that glomerular filtration rates did not alter during the tests.) It was found that reabsorption of glucose was less than normal at low plasma glucose levels, but higher than normal at the highest plasma glucose levels. While in diabetics with a normal renal threshold reabsorption appeared to have reached a definite maximum at very high plasma glucose levels, this was not so in those with a low threshold, although some depression of reabsorption occurred.

The authors discuss Govaerts's theory (*Brit. med. J.*, 1952, **2**, 175) of the relationship between glucose excretion and plasma glucose level. They obtained a linear graph in 4 cases and found that the slope was less than that for inulin excretion and plasma level. It has been tentatively suggested that at expected maximum tubular reabsorption some glucose may diffuse passively into the plasma from the tubules, so producing a higher value, and at lower plasma glucose levels glucose may diffuse into the tubules from the plasma, thus causing a glycosuria with a plasma glucose level below the normal threshold. This theory will be further examined.

R. St. J. Buxton

556. **Hyperventilation and Pseudohypoglycemic Reactions in Diabetes Mellitus**
M. J. MUSSER, T. H. LORENZ, and G. J. DERUS. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **152**, 1113–1116, July 18, 1953.

The authors, working at the University of Wisconsin Hospitals, investigated the possible causes of pseudohypoglycaemic reactions in diabetes mellitus—that is, reactions occurring in the presence of a normal or raised blood sugar level.

A close similarity was observed between symptoms produced by hypoglycaemia and those produced by hyperventilation in anxiety states. "Unstable" diabetics were therefore chosen for the investigation, but those with true hypoglycaemia or proved cerebral dysrhythmia were excluded. All except one of the 14 patients were taking insulin, and all had "reactions" at least once a day. The electroencephalogram was within normal limits in all cases. The blood sugar level was estimated during the fasting state and during the reactions.

During the hyperventilation test, in which the patient took 30 deep breaths a minute for two minutes, subjective symptoms were recorded. All 14 patients were sensitive to this test; symptoms considered to be identical with those experienced during the pseudohypoglycaemic reactions were observed in over half of them, while the symptoms were very similar in the remainder.

The authors conclude that the hyperventilation syndrome produces symptoms that simulate true insulin reactions, and suggest that this simple clinical test should be used for confirmation. *J. N. Harris-Jones*

557. **Cardiovascular–Renal Disease in Diabetes Mellitus. A Clinical Study.** [In English]
S. AARSETH. *Acta medica Scandinavica* [*Acta med. scand.*] Suppl. 281, 1–252, 1953. 14 figs., bibliography.

GENITAL GLANDS

558. **Turner's Syndrome in the Female. Congenital Agonadism Combined with Developmental Abnormalities**
W. P. U. JACKSON and R. SOUGIN-MIBASHAN. *British Medical Journal* [*Brit. med. J.*] **2**, 368–371, Aug. 15, 1953. 3 figs., 12 refs.

The syndrome of ovarian agenesis, first described by Turner in 1938, and the diagnosis of the condition are discussed, with special reference to 3 cases seen within a few weeks at Groote Schuur Hospital, Cape Town.

The salient features of the condition are undeveloped ovaries and an invariable presenting symptom of primary amenorrhoea. The vagina, uterus, and breasts are infantile, pubic hair scanty, but libido is normal. The patient's stature is short (but not like that of the hypopituitary dwarf) and the build is stocky; a "shield-like" chest and a webbed neck are usually present. Associated anomalies involving eyes, ears, and aorta are frequently found. The authors consider that these features are so characteristic of the syndrome that the diagnosis can readily be made without resource to laparotomy or the demonstration of an increase in the level of pituitary gonadotrophin in the urine. They cite the case of a girl aged 9 years 9 months in whom the clinical picture was characteristic and a diagnosis of primary ovarian agenesis was made in the absence of any special investigation.

It is suggested that a germinally defective soma is responsible for the multiple congenital anomalies and that the osteoporosis and hypertension are due to deficiency of oestrogen. Adrenal function was tested in the other 2 cases, normal responses being obtained.

D. W. Higson

559. **Turner's Syndrome in the Male**
R. SOUGIN-MIBASHAN and W. P. U. JACKSON. *British Medical Journal* [*Brit. med. J.*] **2**, 371–372, Aug. 15, 1953. 2 figs., 17 refs.

A case of primary gonadal deficiency in the male, associated with an increase in the gonadotrophin level in the urine, is described. The patient, a man of 30 years, was small in stature, with well-developed muscles and marked webbing of the neck. The genitalia appeared normal, but no erection or emission had been experienced. There was generalized osteoporosis.

It is pointed out that in the female lack of Graafian follicles means germinal and endocrine deficiency, but that in the testis of the male the germinal and endocrine tissues are separate. A table lists the theoretical features of pure germinal agenesis, pure testicular endocrinal agenesis, and a mixture of both. The authors compare the features observed in 5 reported cases of Turner's syndrome in the male with those of the Klinefelter–Reifenstein–Albright syndrome. *D. W. Higson*

560. **Testosterone Phenyl Propionate (TPP): Biological Trials with a New Androgen**
J. DEKANSKI and R. N. CHAPMAN. *British Journal of Pharmacology and Chemotherapy* [*Brit. J. Pharmacol.*] **8**, 271–277, Sept., 1953. 9 figs., 10 refs.

The Rheumatic Diseases

561. **Effect of Short-term Administration of Corticotropin in Active Rheumatic Carditis**
M. G. WILSON, H. N. HELPER, R. LUBSCHEZ, K. HAIN, and N. EPSTEIN. *American Journal of Diseases of Children* [*Amer. J. Dis. Child.*] **86**, 131–146, Aug., 1953. 7 figs., 9 refs.

The results of administration of corticotrophin (ACTH) for short periods (average 7 days) to 28 patients with active rheumatic carditis are reported from New York Hospital. As judged by the clinical findings and the results of fluoroscopic examination the attack was quickly arrested in 24 cases in which the eosinophil count was maintained below 10 per c.mm. (treatment considered "adequate"). In 4 of 8 cases in which the eosinophil count rose above 10 per c.mm. (treatment considered "inadequate"), there was a recurrence of symptoms after treatment was discontinued. The arrest of the carditis was more prompt and complete when treatment was begun within 10 days of the onset of the attack; when treatment was started later there was no reversal of cardiac enlargement. During the follow-up period 3 patients had recurrent attacks; this incidence, the authors point out, is no greater than might be expected. In the authors' view these observations indicate that short-term ACTH therapy is followed by arrest and termination of active carditis, and that it favourably alters the natural course of the disease. *B. E. W. Mace*

562. **Serum Diphenylamine Reaction in Rheumatic Fever**
A. F. COBURN, L. V. MOORE, and J. HANINGER. *Archives of Internal Medicine* [*Arch. intern. Med.*] **92**, 185–188, Aug., 1953. 2 figs., 2 refs.

It has been reported (Niazi and State, *Cancer Res.*, 1948, **8**, 653) that the patient's serum in several disease states contains increased levels of a substance giving a purple colour with diphenylamine. This reaction is measured by the intensity of the colour when serum is added to the diphenylamine reagent. At the Rheumatic Fever Research Institute (Northwestern University), Chicago, raised values were obtained with serum from patients in the acute stage of rheumatic fever, while serum from patients who had recently recovered and others who had shown no signs of activity for one year gave normal values. The intensity of this colour reaction and the erythrocyte sedimentation rate showed close parallelism. The substance in the serum reacting with diphenylamine is unknown, but the authors claim that connective tissue is a rich source of the substance, and that its concentration in the blood is related to the intensity of the inflammatory process.

[Yet another empirical test is added to the already existing battery of tests, with no proof of its superiority over any of the older methods of assessment of activity in rheumatic fever.] *G. Loewi*

563. **Spondylosis Hyperostotica.** (Über die Spondylosis hyperostotica)
V. R. OTT. *Schweizerische medizinische Wochenschrift* [*Schweiz. med. Wschr.*] **83**, 790–799, Aug. 22, 1953. 13 figs., 28 refs.

The author here reports the cases of 11 men and 4 women ranging in age from 44 to 78, who complained of pain in the cervico-dorsal spine of varied duration. Radiography showed typical calcification of the anterior longitudinal spinal ligament, giving an appearance which has been likened to that of sugar-icing. These changes were best seen in the cervical and mid-dorsal spine; they are not to be confused with those occurring in spondylitis ankylopoietica or chronic fluorine poisoning.

In contrast to Forestier and Rotés, who in 1950 described a similar condition under the name of *hyperostose ankylosante sénile* and believed it to be confined to males, the author is able to include 4 females in his series. He rightly points out that this spondylosis of middle and old age is the condition first described by von Bechterew, while the priority for describing ankylosing spondylitis belongs to Strümpell and Marie. A further point of difference between the two conditions lies in the pathogenesis. Ankylosing spondylitis is to be reckoned among the inflammatory diseases, this word being used in its widest sense, while the disease described in this paper belongs to the degenerative arthroses.
L. Michaelis

564. **The Treatment of Osteoarthritis with "Butazolidin" [Phenylbutazone].** (Die Behandlung der Arthrosis deformans mit Butazolidin)
G. NATTERER and K. SCHAAL. *Deutsche medizinische Wochenschrift* [*Dtsch. med. Wschr.*] **78**, 1100–1102, Aug. 14, 1953. 1 fig., 34 refs.

The authors have treated 80 cases of chronic joint disease, of which 68 were cases of osteoarthritis (mainly of the knees) with phenylbutazone ("butazolidin"). The drug was injected intramuscularly in doses of 1 g. as a 20% solution to which a local analgesic had been added, and there were few local or general reactions. The effect was apparent in some cases within 30 minutes, though usually 12 to 24 hours were required. In 12 cases the effect lasted 1 to 3 days, in 48 cases 1 to 2 weeks, and in 16 cases 4 weeks or longer. The average number of injections given was between 2 and 3. Improvement, both objective and subjective, was noted, the greatest benefit being obtained in arthritis of the knees and the least when the spine was affected. Of the 80 patients treated, 24 derived prolonged benefit, 52 substantial relief, and 4 were unaffected.

(In an addendum it is stated that the number of cases treated has subsequently risen to 220, the results obtained being similar to those in the smaller group.)
D. Preiskel

RHEUMATOID ARTHRITIS

565. **Treatment of Rheumatoid Arthritis with *p*-Aminobenzoate and Acetylsalicylic Acid**
C. J. D. ZARAFONETIS, W. A. STEIGER, I. W. GINSBURG, and A. J. HEATHER. *Archives of Internal Medicine* [*Arch. intern. Med.*] **92**, 204–215, Aug., 1953. 1 fig., 11 refs.

This study was made on 44 patients suffering from chronic rheumatoid arthritis of long standing and who were showing signs of deterioration. The investigation was conducted by three separate groups of workers in two different cities (Philadelphia and Wilmington, Delaware) and was carried out mainly on out-patients. Quite apart from the two drugs being tested, namely, *p*-aminobenzoic acid and acetylsalicylic acid, some patients received doses of cortisone, " rarely exceeding 25 mg. per day ", and 3 patients were given physiotherapy. Potassium *p*-aminobenzoate was given in 6 doses per day, each consisting of 2 g., while 0·6 g. of acetylsalicylic acid was given 4 times a day.

It is stated that 34 of the patients were improved, but that 3 months elapsed from the beginning of treatment until the improvement became apparent. This was characterized by a decrease in joint pain, heat, swelling, and tenderness, and in nodule size, and increased freedom of movement, with loss of fever and gain in weight [but no detailed results are given].

[This report indicates that treatment with a combination of the drugs named may be of some value. However, the manner in which this trial was conducted does not allow definite conclusions to be drawn.]

G. Loewi

566. **Thiosemicarbazone in Rheumatoid Arthritis.** [In English]
M. VIRKKUNEN and L. LEHTINEN. *Annales medicinae internae Fenniae* [*Ann. Med. intern. Fenn.*] **42**, 249–256, 1953. 1 fig., 14 refs.

The literature on the use of thiacetazone (thiosemicarbazone) in the treatment of tuberculosis and rheumatoid arthritis is reviewed. Heilmeyer found that administration of thiacetazone in rheumatoid arthritis was followed by a rapid fall in the erythrocyte sedimentation rate (E.S.R.), with a remission in joint symptoms. He suggested that the drug had a cortisone-like effect which it exerted by blocking mineralocorticoids and increasing the action of glycocorticoids. The object of the present investigation, which was carried out at the Kivelä Hospital, Helsinki, was twofold: (1) to determine the effect of thiacetazone in rheumatoid arthritis; and (2) to determine whether this drug acted synergistically with cortisone—for example, by exerting a toxic effect on the liver and delaying cortisone catabolism.

A daily dose of 0·2 to 0·3 g. of thiacetazone was given for an average of 80 days to 37 patients suffering from rheumatoid arthritis, 4 of the patients receiving both thiacetazone and cortisone. Although considerable improvement was observed, in 26 of the 37 patients this was transient, relapse following when administration of the drug ceased. The E.S.R. fell markedly in most of the patients but rose again when treatment was discontinued. Toxic reactions, which were noted in 25 patients, included nausea and vomiting, skin rash, granulocytopenia, albuminuria, and urobilinuria; in 5 cases treatment had to be stopped because of severe nausea. It was found that toxic reactions were closely related to the size of the dose, none being observed when the dose of thiacetazone was less than 0·2 g. daily. No evidence of a synergistic action was found in the 4 patients who received both thiacetazone and cortisone.

The authors conclude that the transient effect of thiacetazone and the serious toxic reactions render this drug of little value in the treatment of rheumatoid arthritis. [There was no control investigation.]

W. Tegner

567. **Practical Experience with Hydrocortisone.** (Praktische Erfahrungen mit Hydrocortone)
A. BÖNI. *Praxis* [*Praxis*] **42**, 702–704, Aug. 20, 1953. 4 refs.

After quoting the results claimed by other workers in the treatment of chronic articular rheumatism with intra-articular hydrocortisone, the author reports his own experience at the Institute for Physical Therapy of the University of Zürich in 18 cases of rheumatoid arthritis. The dose of hydrocortisone given at each injection was 5 mg. for finger and toe joints, 10 mg. for the hands and feet, 20 mg. for the elbow, 20 to 30 mg. for the shoulder, and 40 to 50 mg. for the knee. However, no attempt was made at local treatment until the general health of the patient had been improved as far as possible by other means, such as blood transfusion, gold injections, and administration of cortisone, and only those joints which did not yield to these general measures were injected with hydrocortisone.

A detailed analysis of the results is difficult in view of the polytherapy used, but several individual cases are described. In general, relief of pain and swelling resulted from the injection, enabling effective physiotherapy to be carried out. Injections had to be repeated at intervals of 10 to 14 days, though the interval could usually be gradually extended. Some patients were fortunate in that the local inflammatory reaction cleared up after only one or two injections, but in one case quoted 105 injections into 8 joints were required.

In the opinion of the author, the intra-articular injection of hydrocortisone is not enough by itself, its effect being entirely local.

D. Preiskel

568. **Treatment of Rheumatoid Arthritis with Aurothioglycanide (Lauron)**
R. C. BATTERMAN. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **152**, 1013–1018, July 11, 1953. 4 refs.

It is pointed out that the results of prolonged treatment of rheumatoid arthritis with cortisone and ACTH leave much to be desired. Though there is good functional improvement, the degree of improvement in terms of rheumatoid activity is usually Grade 2 (major) or Grade 3 (minor), rarely Grade 1 (complete remission).

The author, from New York Medical College, describes his experiences with a gold preparation, aurothioglycanide ("lauron"), in the treatment of 69 patients over a period of 8 years. If the disease was recent in onset and not very active 25 mg. was given; this dose was always given initially if the patient had had toxic effects from gold therapy previously. The majority of patients received 50 mg. initially, this initial dose being given once a week for 3 weeks. If no improvement or toxic effects occurred the dose was then doubled, and again increased, if necessary, at 8 or 10 weeks; it never exceeded 150 mg. weekly. This dosage level was continued until improvement was well established, but if after 6 months there was no improvement, treatment was discontinued. In one group of patients who improved treatment was discontinued, while in another a maintenance dose of 50 to 150 mg. at 2- or 4-weekly intervals was given. The total duration of therapy varied between 5 weeks and 3 years.

Altogether 26 patients, regardless of the stage of the disease, showed improvement during the initial phase of treatment. When patients with early arthritis (Stage 1 or Stage 2) were considered, it was found that in just over one-half there was complete remission or major improvement. This initial response was further enhanced by maintenance therapy, since in 15 out of 17 there was a satisfactory end-result.

A comparison of the incidence of toxic effects and their severity with those observed in a series of patients receiving aurothioglucose in another clinic suggested that aurothioglycanide was less toxic. *C. E. Quin*

569. **Urinary Steroid Excretion in Rheumatoid Arthritis. Changes in Ketonic and non-Ketonic Fractions during Hormone Therapy**

A. E. KELLIE and A. P. WADE. *British Medical Journal* [*Brit. med. J.*] **2**, 594–598, Sept. 12, 1953. 6 figs., 12 refs.

In continuation of the study reported by Copeman *et al.* (*Brit. med. J.*, 1952, **1**, 397; *Abstracts of World Medicine*, 1952, **12**, 79) the authors now give further details of 17-ketosteroid excretion following cortisone administration, and also report changes following ACTH therapy. A new method of analysing the non-ketonic fraction has revealed changes not previously reported. The work was carried out at the Middlesex Hospital Medical School, London. Urine was collected from normal male and female subjects, and from patients with rheumatoid arthritis before and during treatment with ACTH and cortisone. The benzene extract of the urine hydrolysate was fractionated by the usual methods and the final fractions (ketonic alcohols, ketonic non-alcohols, non-ketonic 3α-alcohols and non-ketonic 3β-alcohols) were analysed chromatographically. The non-ketonic fractions were assayed by conversion of the alcohols to 3:5-dinitrobenzoates (Kellie *et al.*, *Biochem. J.*, 1953, **53**, 578).

Comparison of the steroid excretion in the normal subjects and in untreated arthritic patients showed that: (1) the aetiocholanolone:androsterone ratio is higher in the latter, a change already reported in at least one other pathological condition; (2) the ketonic non-alcohols are unchanged; (3) the non-ketonic 3α-alcohols (probably mono-, di, and tri-hydroxy alcohols) are considerably reduced in quantity; (4) the amount of non-ketonic 3β-alcohols excreted in both normal and rheumatoid arthritic subjects was negligible.

A close study was made of 3 arthritic patients who were receiving hormone therapy, namely, ACTH, cortisone, and ACTH followed by cortisone respectively. The administration of ACTH led to a great increase in steroid excretion, which was reflected in all fractions but was mainly due to increased output of androsterone and aetiocholanolone. Treatment with cortisone was followed by an irregular small rise in 17-ketosteroid excretion, mainly in the ketonic alcohols and particularly aetiocholanolone; it is pointed out that this finding is contrary to that of other workers. *Nancy Gough*

570. **Combined Treatment of Rheumatoid Arthritis with Cortisone and "Butazolidin" [Phenylbutazone].** (Kombinationstherapie bei chronischer Polyarthritis mit Cortison und Butazolidin)

O. GSELL and H. K. VON RECHENBERG. *Schweizerische medizinische Wochenschrift* [*Schweiz. med. Wschr.*] **83**, 1079–1082, Nov. 7, 1953. 2 figs., 20 refs.

COLLAGEN DISEASES

571. **Progressive Systemic Sclerosis (Scleroderma)**

P. M. BEIGELMAN, F. GOLDNER, and T. B. BAYLES. *New England Journal of Medicine* [*New Engl. J. Med.*] **249**, 45–58, July 9, 1953. 7 figs., 30 refs.

In this paper 15 cases of progressive systemic sclerosis (scleroderma) are described in detail from the Peter Bent Brigham and Robert Breck Brigham Hospitals, Boston. The average age of onset was 40 (range 19 to 52) and all but 3 patients were women. All 15 had constitutional symptoms, and showed the characteristic thickening of the skin of the hands. The authors were impressed by the frequent involvement of other systems; for example, in 12 patients there was joint pain or swelling, 14 patients had cardio-respiratory embarrassment, and in 11 patients there were gastro-intestinal symptoms. The majority had abnormal signs in the heart and lungs, the chest radiographs of 7 patients showing abnormalities mainly linear streaking at the bases and alteration of the cardiac outline. Electrocardiographic changes were common; these were largely non-specific and included inverted T waves, low-voltage complexes, and arrhythmias. Post-mortem examination of 5 of the 6 fatal cases confirmed the widespread visceral changes typified by microscopic fibrosis in the myocardium, lungs, gastro-intestinal tract, kidneys, and liver. Corticotrophin and cortisone therapy was tried in 9 cases, but only one patient seemed to benefit. Other treatment with metals, hormone preparations, vitamins, and peripheral vasodilators gave consistently negative results.

The authors suggest that in view of the widespread distribution of the lesions in scleroderma and of the histological findings, this disease must be regarded as an

antigen–antibody allergic reaction of the mesenchymal tissues, resembling acute disseminated lupus erythematosus in this respect, but differing from it in its slow response to the allergic reaction and in the predominance of fibrosis and sclerosis. One of the authors' patients presented simultaneously some of the features of both diseases, indicating in their opinion a relationship between the two. *K. C. Robinson*

572. **Serum Complement in Children with " Collagen Diseases "**

R. J. P. WEDGWOOD and C. A. JANEWAY. *Pediatrics* [*Pediatrics*] **11**, 569–581, June, 1953. 8 figs., 27 refs.

The authors give details of a new spectrophotometric method developed at the Children's Medical Center (Harvard Medical School), Boston, for the determination of a 50%-haemolytic end-point in the estimation of serum complement. Using this technique, which they consider to be far more sensitive than the normal routine methods at present in use, they studied the quantitative changes in serum complement level in 70 children suffering from various collagen diseases. The initial figures were below normal in lupus erythematosus (4 cases), acute glomerular nephritis (20), and nephrosis (15), and greater than normal in anaphylactoid purpura (14), dermatomyositis (6), and rheumatoid arthritis (11). In the three disorders in which the serum complement value was initially low, a rise occurred in association with clinical improvement, however induced. There was no evidence of anti-complementary activity in the serum. The low serum complement level before treatment cannot be explained as the result of protein loss during the acute phase as there was no correlation between the degree of urinary protein excretion and the serum complement level, and would appear to support the theory that these diseases are allergic in nature, serum complement being depleted by certain gross antibody–antigen reactions. The significance of the high serum complement values in rheumatoid arthritis, dermatomyositis, and rheumatic fever is discussed, and it is suggested that such findings do not exclude the possibility of an immunological mechanism in the pathogenesis of these diseases; the differences in serum complement titres may reflect differences in the relative quantities, types, or location of the antigens and antibodies involved, or in the time relations between stimulus and reaction. *R. E. Tunbridge*

573. **The Natural History of Lupus Erythematosus and its Modification by Cortisone and Corticotrophin (A.C.T.H.)**

H. COHEN and E. F. B. CADMAN. *Lancet* [*Lancet*] **2**, 305–312, Aug. 15, 1953. 4 figs., bibliography.

In this paper from the University of Liverpool the natural history of lupus erythematosus is discussed and the close relationship between the chronic discoid and acute systemic forms of the disease is demonstrated by reference to 16 cases.

The typical chronic discoid rash was observed in 9 cases of lupus erythematosus. On pathological examination no evidence of an increase in the erythrocyte sedimentation rate (E.S.R.) was found and tests for the presence of L.E. cells were negative. Minor abnormalities included leucopenia and an increase in the serum globulin level. In a further group of 7 cases major systemic reactions were observed. One patient, a woman aged 47 years, suffered from chronic discoid lupus erythematosus for 2 years before systemic changes, such as arthritis, pleural effusion, and loss of weight, were noted. After these symptoms had subsided L.E. cells were still present in the blood. In the remaining 6 cases in this group the systemic manifestations were increasingly severe. The authors believe that the evidence presented by these cases favours a unitary conception of the disease—for example, the typical chronic discoid rash developed in a woman, aged 40 years, with rheumatoid arthritis, hepatosplenomegaly, pyrexia, leucopenia, and a raised E.S.R.

The response to administration of cortisone or ACTH was minimal in patients suffering from the chronic discoid form of the disease; on the other hand, there was a dramatic improvement in response to these drugs in 4 patients with systemic lupus erythematosus. Cortisone was given by mouth in a dose of 25 mg. 4 times a day and ACTH by intramuscular injection in a dose of 25 mg. every 6 hours. All except one of the patients were finally maintained on a daily dose of cortisone which ranged from 37·5 to 75 mg. a day, the exception being a patient who received a maintenance dose of 10 international units of ACTH gel at intervals of one week. Although permanent remission was not obtained, the authors believe that such hormone therapy is justified in the cases of acute systemic disease. This treatment should not, however, be given to patients with a mild form of the disease, for spontaneous remissions are obtained less readily in such cases; moreover, hormone therapy may precipitate a systemic spread in patients with chronic discoid lesions. *A. Garland*

574. **Some Effects of Nitrogen Mustard and Triethylene Melamine in Acute Disseminated Lupus Erythematosus**

R. J. ROHN and W. H. BOND. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **226**, 179–190, Aug., 1953. 2 figs., 18 refs.

As difficulty is often encountered with the use of corticosteroids in the treatment of disseminated lupus erythematosus, 5 patients at the Indiana University Medical Center, Indianapolis, were treated with nitrogen mustard, 2 receiving triethylene melamine as well. The duration of remission of signs and symptoms after administration of these drugs varied from 6 days to a maximum of 217 days, as compared with 14 to 300 days after treatment with ACTH. Since in most of the patients there was impaired bone-marrow function as the result of the disease the total dosage of nitrogen mustard was limited to 0·4 mg. per kg. body weight. The authors do not consider that nitrogen mustard and triethylene melamine are effective solely through adrenal cortical stimulation; their mode of action, therefore, must remain in doubt. It is suggested that treatment with nitrogen mustard in combination with corticosteroids might be beneficial in these cases.

Geoffrey McComas

Traumatic Surgery and Orthopaedics

575. **Studies on Allergic Reactions following Administration of Dextran.**
H. HEISTØ and I. LUND. *Journal of the Oslo City Hospitals* [*J. Oslo City Hosp.*] **3**, 159–170, July–Aug., 1953. 4 figs., 13 refs.

Eight different preparations of dextran were given a clinical trial at Ullevål Hospital, Oslo. The authors stress the importance of selecting subjects in normal health for such a test. Each of 29 volunteers was given an infusion of 1 litre of one of the preparations, which contained amounts of dextran ranging from 5·49 to 6·2 g. per 100 ml. Reactions of an allergic nature occurred in 15 patients. In mild cases this consisted of flushing of the face and neck and a sensation of warmth; in more severe cases there was extensive urticaria, rashes, malaise, pyrexia, headache, or vomiting. Previous typhoid–paratyphoid A and B inoculations, particularly when recent, predisposed the subjects to a reaction. When reactions occurred there was always some decrease in the plasma volume and a marked fall in the total plasma protein level; the albumin:globulin ratio, however, remained constant. When no reactions followed the infusion, the expected increase in plasma volume was observed.

It is believed that the strain of *Leuconostoc mesenteroides* used in the production of these dextran preparations, rather than the technique of preparation, may have been responsible for these reactions, batches from old strains producing allergic symptoms in nearly every case during the trial. *J. S. Campbell*

576. **Late Results of Treatment of Congenital Dislocation of the Hip**
G. M. MULLER and H. J. SEDDON. *Journal of Bone and Joint Surgery* [*J. Bone Jt Surg.*] **35B**, 342–362, Aug., 1953. 4 figs., 10 refs.

This is a detailed statistical analysis of 264 cases of congenital dislocation of the hip treated at the Royal National Orthopaedic Hospital, London, in the period 1891–1940. The cases analysed are those in which the patient was traced and examined during the years 1949–50, and are regarded as presenting a more favourable picture than would probably be found in the whole series of 889 cases treated during the 50-year period. [The report does not easily lend itself to condensation and the reader is recommended to study the original. Some of the conclusions drawn by the authors are summarized below.]

The results of closed reduction gave " reason for sober satisfaction ", being satisfactory in four-fifths of the unilateral cases and in two-thirds of the bilateral cases if treatment was instituted before the age of 3 years. Immediate open reduction gave only moderate results in the 9 cases studied. Of secondary operative procedures, the shelf operation was the most successful, giving encouraging results in two-thirds of the cases. In general, the outcome of open reduction was bad, the results being satisfactory in only 4 out of 20 cases. Rotation osteotomy " presented a dismal picture " having been effective in only 4 out of 9 cases. The effective life of the successfully treated hip appears to be between 25 and 30 years, after which the joint becomes troublesome in about 50% of cases. *John Charnley*

577. **Operative Treatment of Recurrent Dislocation of the Shoulder Joint with Formation of an Intra-articular Ligament.** (Оперативное лечение привычных вывихов плеча путем создания внутрисуставной связки)
G. A. ORLOV. *Хирургия* [*Khirurgiya*] 67–70, No. 5, May, 1953. 2 figs.

The author describes his operative treatment for recurrent dislocation of the shoulder joint. In this operation the tendon of the long head of the biceps is divided, its proximal end being brought out through a tunnel drilled in the humeral head, where it is split and fixed to the periosteum of the humerus; the distal end of the tendon is attached to the edge of the deltoid muscle. The living tendon provides an intra-articular ligament, and the long head of the biceps preserves its physiological function of helping to elevate and abduct the arm.

The author believes that his technique gives greater strength and stability to the shoulder joint than does the Nicola operation. In 11 of his patients treated by this technique and followed up for 1 to 9 years the results were excellent. *Z. W. Skomoroch*

578. **Hip Deraagements Seen in Cerebral Palsied Children**
S. S. MATHEWS, M. H. JONES, and S. C. SPERLING. *American Journal of Physical Medicine* [*Amer. J. phys. Med.*] **32**, 213–221, Aug., 1953. 7 figs., 4 refs.

The authors record and discuss cases of hip-joint deformity observed during routine examinations at the Cerebral Palsy Clinic of the Children's Hospital, Los Angeles, between 1947 and 1952. Among 1,243 patients, ranging in age from infancy up to 19 years, 162 with clinical signs suggestive of hip-joint derangement were noted, and radiographic evidence of abnormality was found in 32 (2·6%). The deformity was congenital in type in 6 and non-congenital in 26 (8 with dislocation and 18 with subluxation or migration of the femoral head). Cases of the latter type were characterized by a valgus position of the femoral head and neck with relation to the shaft with an angle of 150 degrees or more in 23 cases, tear-drop deformity of the head in 15 cases, and normal acetabulum in all. The majority of the patients suffered from severe spastic quadriplegia, and 15 of them had never stood or walked to any

appreciable extent. Sex distribution was equal, and half were under 5 years of age. Typically, the flexor, adductor, and internal rotator muscles of the hip were stronger, tighter, and more spastic or rigid than those of the opposing groups.

In the majority of cases operative treatment would have had little hope of success either on account of the severity of the condition or the low intelligence of the patient. In 6 cases of the non-congenital group with migration of the femoral head, however, tenotomy of the adductor longus muscle and neurectomy of the anterior branch of the obturator nerve were performed, followed by straight traction in wide abduction, and resulted after 4 months in a satisfactory position of the femoral head, improvement in walking or standing, and facilitation of nursing care. The authors recommend periodic *x*-ray examination of the pelvis in all cases of cerebral palsy, and are of the opinion that whenever a valgus of the femoral neck of more than 150 degrees is present, early dislocation of the hip joint may be expected.

V. Reade

579. **The Normal Vascular Anatomy of the Femoral Head in Adult Man**

J. TRUETA and M. H. M. HARRISON. *Journal of Bone and Joint Surgery* [*J. Bone Jt Surg.*] **35B**, 442–461, Aug., 1953. 31 figs., 34 refs.

In an investigation at the Nuffield Orthopaedic Centre, Oxford, of the blood supply to the femoral head in 36 adult specimens obtained post mortem, injections of barium sulphate suspension, silver iodide solution, Berlin blue, and " neoprene latex " solution were made into the medial circumflex femoral artery, the common femoral artery, or the common iliac artery. The barium-sulphate and silver-iodide methods permitted radiological examination of the specimen, either complete or after sections had been made. Latex casts of the vascular tree, obtained by digestion of the bone and marrow with acid, were dissected under water.

It was found that the vascular patterns established during growth and delineated by the cartilaginous epiphysial plate persist throughout adult life, and the vessels entering the head may thus be termed metaphysial or epiphysial, after the origin of the area which they supply. From the medial circumflex femoral artery arise superior and inferior metaphysial and lateral epiphysial vessels, and from the acetabular branch of the obturator artery a branch passes along the ligamentum teres to form the medial epiphysial artery. The lateral epiphysial vessels, 2 to 6 in number, enter the femoral head posteriorly in a thick fibrous sheath, passing transversely above the epiphysial scar to supply most of the head of the bone. The medial epiphysial artery enters the pit on the head of the femur, supplies a small area of surrounding bone, and anastomoses with the lateral epiphysial system. The final distribution of the epiphysial vessels is through a series of radially-arranged vessels which unite to form arcades as they pass towards the articular cartilage. On the upper aspect of the femoral neck 2, 3, or 4 superior metaphysial arteries enter the bone. These pass at first vertically downwards, and then turn medially towards the epiphysial scar. The inferior metaphysial arteries enter the under surface of the neck close to the articular cartilage. The metaphysial and epiphysial circulations anastomose across the epiphysial scar, the anastomotic vessels often showing a spiral formation.

These investigations did not demonstrate any diminution in the blood supply to the femoral head with advancing age. The situation of the main epiphysial arteries laterally may explain why these vessels are more liable to injury in adduction than in abduction fractures of the femoral neck and the higher incidence in the former of avascular necrosis of the head of the femur.

Peter Ring

580. **A Contribution to the Problems of the Aetiology and Pathogenesis of Taratinov's Disease (Eosinophilic Granuloma of Bone or Benign Medullary Reticuloma with Eosinophilia).** (К вопросу об этиологии и патогенезе болезни Таратинова (эозинофильная гранулома костей или доброкачественная костномозговая ретикулома с эозинофилией)).

N. I. SOBOLEVA and A. I. PYABINKINA. *Архив Патологии.* [*Arkh. Patol.*] **15**, 37–46, July–Aug., 1953. 6 figs., 12 refs.

The authors discuss 11 personal cases of eosinophilic granuloma of bone. The distribution of the lesions was as follows: the bones of the skull in 4 cases, the femur in 2 (in one of which there was also a lesion in the acromial process), and the ribs, humerus, scapula, tibia, and ilium in one case each. In one of the patients, in whom the initial lesion was in the skull, new foci were observed 2 months later in the bones of the head, and a year later in both iliac bones. The case in which simultaneous lesions appeared in both the femur and acromion showed a new focus 2 months later in the left parietal bone, while the patient in whom the rib was affected, 6 months later showed another focus in the head of the humerus. Thus there were altogether 3 cases with multiple lesions.

In 6 of the cases there was a peripheral blood eosinophila of 7 to 19%, the total leucocyte count " in most cases " being between 9,000 and 10,000 per c.mm. The patients' ages ranged from 11 months to 27 years, and 6 of them were between 3 and 5 years of age. Histologically, the principal components were large, pale reticulum cells, in places forming solid sheets. Among these, giant cells were frequently observed. Eosinophils were seen in almost all microscope fields, either diffusely infiltrating the reticular tissue or forming aggregates.

Pain in the affected bones was a prominent symptom. The treatment included scraping out the lesions, this being followed by a course of penicillin and in 4 cases also by radiotherapy. The scraped-out foci healed well, with new bone formation in all surviving cases. One patient died on the 8th day after operation from suppurative meningitis. The authors regard eosinophilic granuloma as a border-line phenomenon between hyperplasia and neoplasia, and propose to call it " Taratinov's disease ", after a Russian scientist who described it in 1914.

A. Swan

Neurology and Neurosurgery

581. **Adenosine-5-monophosphate in the Treatment of Multiple Sclerosis**
M. L. LOWRY, R. W. MOORE, and R. CAILLIET. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **226**, 73–83, July, 1953. 20 refs.

Pursuing a theory that disseminated sclerosis may be, in part at least, due to a nutritional deficiency, the authors treated 14 cases of long standing with intramuscular injections of adenosine-5-monophosphate. In 3 cases the effect of iron adenosine-3-monophosphate was also tried. These compounds had no effect on spasticity, incoordination, sensory disturbances, or visual symptoms, the only improvement noted being in energy and sphincter control; with regard to the latter it is of interest that potency was unaffected. *J. Foley*

582. **Fibrillary Chorea of Morvan. Review of 70 Cases Including 30 Personal Cases.** (La chorée fibrillaire de Morvan. Bilan de 70 observations dont 30 personnelles)
H. ROGER, J. ALLIEZ, and J. ROGER. *Revue neurologique* [*Rev. neurol.* (*Paris*)] **88**, 164–173, 1953. 2 refs.

The authors point out that the fibrillary chorea first described by Morvan in 1890 is not so rare as might be supposed, and they give here a review of the 70 cases of which they have knowledge, 30 having been seen by themselves. The clinical features include: (1) fibrillary contractions involving several muscle-fibre groups, giving rise to small undulations which appear to flow under the skin and are quite different from myoclonic jerks, although the latter may, in rare instances, be superadded; they are asynchronous, are made more obvious by exposure to cold, and disappear on voluntary movement; there is no wasting; (2) pains, which may be severe and cramp-like, or simple paraesthesiae; (3) psychic disorders, usually of a depressive, anxious, and irritable nature, sometimes severe enough to be the presenting symptom; intractable insomnia is very common; (4) a cutaneous syndrome, comprising sudoral crises, acrodynia, and pruritus; (5) a cardiovascular syndrome of tachycardia and mild hypertension, present in about 50% of cases. Examination shows no objective signs of disorder in the central nervous system, and the cerebrospinal fluid and electroencephalogram are usually normal. There is little in the way of general signs, no fever, and a normal blood picture. The sexual potency and menstrual periods may be disturbed, and a moderate loss of weight is normal. The course of the disease is long (4 months on average), but usually benign, although some cases complicated by definite neurological abnormalities have been fatal. Two cases have relapsed after 2 to 4 years, and some have remained subacute for 4 to 10 years. The combination of fibrillary contractions with neurovegetative disturbances and the absence of muscular wasting makes the diagnosis fairly simple to those aware of the disease, but in the early stages fibrillary contractions may not be present and the case may be diagnosed as one of functional disorder.

The authors consider it probable that the disease is a result of some process affecting the vegetative centres of the diencephalon, and they discuss the possibilities of an infectious, toxic, or allergic pathogenesis. In particular they point out that the similarity of the cutaneous manifestations to those of infantile acrodynia (pink disease) has led to the suggestion that the latter is an infantile variant of Morvan's fibrillary chorea. The results of treatment have been disappointing, but it is suggested that BAL might be of help in view of the possible aetiological connexion between infantile acrodynia and heavy-metal poisoning. *J. B. Stanton*

583. **The Cerebrospinal Fluid Pressure as an Aetiological Factor in the Development of Lesions Affecting the Central Nervous System**
J. E. A. O'CONNELL. *Brain* [*Brain*] **76**, 279–298, 1953. 5 figs., 18 refs.

In this paper, in which he discusses the role of the cerebrospinal fluid pressure in the development of lesions affecting the central nervous system, the author recalls that the pressure of the cerebrospinal fluid (C.S.F.) depends on the balance of the forces responsible for its production and its reabsorption, this balance being modified by cardiac and respiratory activity. The fluctuations in pressure due to these causes are probably considerably greater than is generally realized, since it is usual to use small-bore needles and a slowly responding manometer system to record them. Measurements are given of ventricular pressure which were obtained with a wide-bore brain needle and which suggest that the total fluctuation may be as much as 80 mm. of spinal fluid; this occurs because the amount of blood contained in the intracranial veins varies, causing changes in pressure of the C.S.F. Thus the rise in pressure as a result of forced expiration may be over 300 mm. of fluid, and is higher than that due to jugular compression. These effects provide the explanation for the papilloedema that may occur with chronic bronchitis and emphysema or similar conditions. High venous pressure is probably also the cause of the papilloedema seen in polycythaemia rubra vera.

The considerable fluctuations in the pressure of the C.S.F. are also thought to cause the formation of spinal extradural and subarachnoid cysts. Reports of such cysts found during explorations for suspected intervertebral-disk lesions are presented.

The third type of lesion considered is the chronic subdural haematoma. It is suggested that such a haematoma is formed because the intracranial C.S.F. pressure is sub-atmospheric in the upright position. A parallel is drawn with the formation of a pneumothorax due to sub-atmospheric pleural pressure. Much supporting

evidence is advanced for this hypothesis: for example, the fact that relatively large amounts of fluid may collect without signs of raised intracranial pressure.

Donald McDonald

BRAIN AND MENINGES

584. **The Prognostic Value of the *p*H of the Cerebrospinal Fluid in Cranial Trauma and in Neurosurgery.** (El *p*H del líquido céfalorraquídeo en los traumatismos de cráneo. Su valor pronóstico. El *p*H del líquido céfalorraquídeo en neurocirugía. Su valor pronóstico en el postoperatorio)

L. RAO. *Prensa médica argentina* [*Pren. méd. argent.*] **40**, 1358–1360, May 29, 1953.

Since 1948 it has been the practice in the author's clinic at the Italian Hospital, Buenos Aires, to drain the ventricles in all cases of severe head injury. It is often found that the intraventricular pressure is very low, indicating a virtual failure of function of the choroid plexus. If drainage of the ventricles causes a resumption of the flow of cerebrospinal fluid (C.S.F.) in the first 24 hours the prognosis is good, but if the failure persists the prognosis is poor. This treatment is in addition to routine measures to maintain the systemic circulation. The *p*H of the C.S.F. has been determined in a series of cases, and the following conclusions have been drawn. If the *p*H is 7·4 or greater, then the prognosis is good and operative interference is not indicated unless there is a haematoma—which is unusual with such a high *p*H. If the *p*H is less than 7·3, then the prognosis is much less good, and where it has fallen below 7·0 the outcome has invariably been fatal in the author's experience. The presence of blood in the C.S.F. is not in itself a bad sign, for the blood acts as a buffer and stabilizes the *p*H.

Similar findings have been obtained after neurosurgical operations. The use of ganglion-blocking drugs to secure circulatory hypotension during operation has been blamed for the failure in C.S.F. secretion which is often found postoperatively, but the author has found no evidence that it is an important factor. The lowest *p*H value recorded after a neurosurgical operation was 6·6, in a case which had a fatal outcome. In general, when the alkalinity of the fluid was maintained, the patient progressed well. *Donald McDonald*

585. **Cervical Sympathectomy in the Treatment of Cerebral Vascular Disorders**

J. L. POPPEN and C. A. FAGER. *Lahey Clinic Bulletin* [*Lahey Clin. Bull.*] **8**, 142–148, July, 1953. 11 refs.

In a group of 25 patients who have undergone cervical sympathectomy for cerebral and carotid thrombosis, only 5 showed some improvement following the operation. These were patients with symptoms of brief duration and they have survived more than three years with no recurrence or progression of symptoms. Twenty patients showed no significant improvement; 8 of these are deceased and 3 died within a few days of sympathectomy.

In the light of these observations it is doubtful that interruption of the sympathetic pathways to the affected side of the brain is of any value in cerebral or carotid thrombosis except, perhaps, in the early stages. If the patient survives, it is possible that sympathectomy may prevent further episodes on the same side.—[Authors' summary.]

586. **Lysivane in the Treatment of Parkinsonism**

R. O. GILLHESPY. *Edinburgh Medical Journal* [*Edinb. med. J.*] **60**, 365–370, Aug., 1953. 5 refs.

"Lysivane" (ethopropazine hydrochloride), which possesses parasympathicolytic, antihistamine, anti-acetylcholine, antinicotine, and anti-adrenaline properties, was given orally at the Dudley Road Hospital, Birmingham, to 100 patients ranging in age from 30 to 80 years and suffering from chronic Parkinsonism of varied aetiology. At first, one tablet containing 50 mg. of the drug was administered every 4 hours and, depending on the effect of the drug, the dose was gradually increased over the next 2 weeks to a maximum of 50 mg. every 2 hours.

Of these 100 unselected patients, 68 showed marked clinical improvement, with relaxation of the rigidity and reduction of tremors sufficient to enable them to return to normal activity. In the remaining 32 there was either no response or the patient's condition deteriorated. Only one patient in the series could not tolerate the drug. Distressing ill-effects observed (in 38 cases) were dryness of mouth, nausea, vomiting, difficulty in visual accommodation, and vertigo. The author, discussing the pharmacology of the drug, suggests that the reduction of muscular rigidity and damping down of tremors is due to the restoration of the balance between the centres in the mid-brain and the higher inhibition, brought on by the selective action of the drug on the acetylcholine transmission of inhibitory and excitatory impulses. He is convinced that lysivane is the drug with the widest application at present available, and that it should be tried in all new cases of Parkinsonism. *S. Karani*

587. **Pneumococcal Meningitis. Skull Defects as an Aetiological Factor**

W. H. GALLOWAY and W. CHAMBERS. *Lancet* [*Lancet*] **2**, 68–70, July 11, 1953. 8 refs.

Of a series of 27 cases of pneumococcal meningitis treated at the City Hospital and elsewhere in the Aberdeen district in 1946–52, trauma to the skull preceded the acute onset of meningitis by many months, or even years, in 6, while in another there was a congenital absence of the cribriform plate. Otitis, pneumonia, or peritonitis were associated with the onset in another 8 cases, no primary source of infection being detected in the remainder.

A combination of sulphonamides and penicillin was used in the treatment, a few patients also receiving streptomycin. Operation was performed on 2 patients with previous fractures of the skull, with good results. There were 9 deaths, including one of the cases of skull defect, and of the 15 survivors who were followed up, recovery was complete in all but 4, one of whom was

totally deaf, another developed acute mania, while 2 others suffered from rhinorrhoea.

It is emphasized that the possibility of some skull defect should never be overlooked in any patient who has recurrent attacks of meningitis. *Adrian V. Adams*

588. **Prognosis in Acute Disseminated Encephalomyelitis ; with a Note on Neuromyelitis Optica**
H. G. MILLER and M. J. EVANS. *Quarterly Journal of Medicine* [*Quart. J. Med.*] **22**, 347–379, July, 1953. 49 refs.

This paper is based on a follow-up study of the survivors among a total of 34 patients with acute disseminated encephalomyelitis admitted to the Royal Victoria Infirmary and the City Hospital for Infectious Disease, Newcastle upon Tyne, between 1932 and 1942, 27 of whom survived for periods varying from 10 to 19 years. The main object was to delineate the natural history of this disease and its relationship to disseminated sclerosis and neuromyelitis optica. Seven of the patients died in the course of the initial attack, 4 to 270 days after its onset, and 5 others died later of unconnected causes. There were 3 cases of relapse and 5 of recurrence of encephalomyelitis. None of the 22 survivors had developed unequivocal disseminated sclerosis, although all but 9 had some residual, non-progressive disability. The series included 3 cases of neuromyelitis optica.

It is held that these findings confirm the view that acute disseminated encephalomyelitis and disseminated sclerosis are two separate diseases with entirely different prognoses. On the other hand, the authors consider that neuromyelitis optica is a variant of acute disseminated encephalomyelitis. *L. Crome*

EPILEPSY

589. **Clinical Significance of Sclerosis of the Cornu Ammonis. Ictal " Psychic Phenomena "**
K. SANO and N. MALAMUD. *Archives of Neurology and Psychiatry* [*Arch. Neurol. Psychiat.* (*Chicago*)] **70**, 40–53, July, 1953. 5 figs., 41 refs.

The brains of 50 epileptic patients dying in two Japanese institutions between 1946 and 1952 were examined at the Langley Porter Clinic, San Francisco, with particular attention to sclerosis in the cornu Ammonis ; their case histories and electroencephalograms were studied for evidence of psychomotor epileptic attacks. In 29 cases sclerosis was found in the cornu Ammonis; in 9 of these there were also lesions in the frontal or temporal lobes, and in 11 there were congenital deformities of the brain; the remaining 9 showed no definite pathological changes apart from those in the cornu. In all 9 patients in the first and in 7 of the second group " ictal psychic phenomena " had occurred, in which rage was a prominent feature.

In 21 cases no changes were found in the cornu, although 7 patients had malformed brains and in 9 there were traumatic lesions in the frontal or temporal lobes. In only 3 of this group was there a history of " ictal psychic phenomena ", and rage was a feature in only one. The authors suggest that in many of these cases the changes in the cornu Ammonis resulted from repeated convulsions, and that the resulting sclerosis became an epileptic focus for temporal-lobe seizures. *J. W. Aldren Turner*

590. **Convulsive Effects of Light Stimulation in Children**
R. G. BICKFORD, D. DALY, and H. M. KEITH. *American Journal of Diseases of Children* [*Amer. J. Dis. Child.*] **86**, 170–183, Aug., 1953. 6 figs., 11 refs.

At the Mayo Clinic 27 epileptic children who were sensitive to flickering light were examined. It was found that 3 separate groups could be recognized: (*a*) patients in whom light of the intensity encountered in daily life induced an epileptic attack; (*b*) less-sensitive patients, in whom an attack could be induced only under laboratory conditions; and (*c*) patients in whom sensitivity was shown only by a change in the electroencephalogram (EEG). There was, however, no specific pattern in the EEG which was diagnostic of the condition. A close relationship was observed between myoclonic jerking and the appearance of spike discharges, the relationship between arrest of speech and spike discharges being more variable. The frequency of experimental flashes of light varied from 1 to 35 per second, the most effective frequencies being between 10 and 20 per second. Certain anticonvulsant drugs when given intravenously suppressed or reduced the sensitivity to flickering light, but the effect was brief. In patients whose epileptic attacks occurred in relation to flickering light the wearing of tinted or " polaroid " spectacles was sometimes effective. *Hugh Garland*

591. **The " Twilight " Attack as the Characteristic Type of Attack in Temporal Epilepsy (Psychomotor Attacks, Epileptic Equivalents, Automatism).** (Die Dämmerattacken als charakteristischer Anfallstyp der temporalen Epilepsie (psychomotorische Anfälle, Äquivalente, Automatismen))
R. W. MEYER-MICKELEIT. *Nervenarzt* [*Nervenarzt*] **24**, 331–346, Aug. 20, 1953. 5 figs., 37 refs.

The author describes " twilight " attacks occurring in 72 cases of temporal epilepsy adequately observed at the University of Freiburg. He defines these as short attacks of altered consciousness, usually accompanied by motor automatism, vegetative symptoms, and aimless behaviour and utterances, occurring as focal attacks in temporal-lobe epilepsy. According to degree and severity, these attacks can be divided into three groups, any of which may occur at different times in the same patient: (1) mild attacks similar to the " absences " of petit mal; (2) attacks with coordinated motor automatism such as swallowing, smacking of the lips, groping, or running about; (3) attacks with severe tonic deviation, often with disturbance of postural tone and falling to the ground. The psychic manifestations range from dreamy states with anxiety and feelings of strangeness to complete unconsciousness with amnesia. Visual hallucinations and *déjà-vu* experiences are common, and auditory hallucinations of voices, sometimes speaking the patient's own

thoughts, may occur. About half the author's patients had a premonitory aura, usually visceral but sometimes olfactory. In addition to these attacks, more than half the patients suffered from major convulsive seizures, and in only one-quarter did the " twilight " attacks occur as the sole epileptic manifestation. In 57 of the cases the attacks were symptomatic of temporal-lobe damage from preceding trauma or infection, or of tumour or vascular damage, and in only 15 (in 4 of which there was a positive family history) was idiopathic epilepsy diagnosed. These attacks appear characteristically (80%) in the middle age groups (21 to 50 years). An abnormality of the electroencephalogram (EEG) was present between attacks in 85% of the patients, with an epileptic focus in one or both temporal regions in 76%.

In the differential diagnosis, a distinction between " twilight " attacks and the " absences " of petit mal can be made clinically by the stereotyped nature of the latter, with absence of aura and psychic manifestations and only uncoordinated myoclonic motor accompaniments, while the characteristic spike-and-wave EEG is conclusive. Differentiation from psychogenic attacks is less easy, resting on the occurrence of an aura and the characteristic psychic experiences in the " twilight " attack. Schizophrenic hallucinations are less likely to be confused with temporal-lobe attacks because of their lack of homogeneity.

The author states that these cases are often difficult to treat, the hydantoinates being on the whole more efficacious than phenobarbitone, and troxidone often making the attacks worse. Only in cases in which the EEG shows a unilateral temporal focus and which are resistant to anticonvulsant therapy should surgical treatment be considered. *J. B. Stanton*

592. **Use of Milontin in the Treatment of Petit Mal Epilepsy. (Three per Second Spike and Wave Dysrhythmia)**
P. J. DOYLE, S. LIVINGSTON, and P. H. PEARSON. *Journal of Pediatrics* [*J. Pediat.*] **43**, 164–166, Aug., 1953. 1 fig., 3 refs.

After a brief reference to the results obtained by other workers, the authors describe their own experience with methylphenylsuccinimide (" milontin ") in the treatment of 21 patients with petit mal epilepsy at the Johns Hopkins Hospital. The attack of petit mal in these patients consisted in a transient lapse of consciousness associated with a bilaterally synchronous 3-per-second spike-and-wave form in the electroencephalogram (EEG). To 8 of the patients paramethadione (" paradione ") and troxidone (" tridione ") had been given previously without benefit. The average duration of milontin therapy was 3 to 4 months, and the dosage of the drug was increased gradually to a maximum of 3 g. daily. No significant side-effects were observed.

Seizures were not entirely controlled in any of the patients; in 2 the number of attacks was reduced by approximately one-half. In 8 of the 13 patients who subsequently received paramethadione or troxidone attacks were completely controlled and the EEG returned to normal.

The authors conclude that milontin is essentially ineffective in the treatment of petit mal associated with a 3-per-second spike-and-wave form in the EEG, and advocate paramethadione and troxidone in such cases. They state that their results are contrary to those obtained by Zimmerman (*Arch. Neurol. Psychiat.* (*Chicago*), 1951, **66**, 156; *Abstracts of World Medicine*, 1952, **11**, 188), who found that milontin was equal if not superior to troxidone in treatment of petit mal, and to those of Millichap (*Lancet*, 1952, **2**, 907; *Abstracts of World Medicine*, 1953, **13**, 321) who, confirmed the efficacy of milontin by a controlled experiment. In these two investigations the clinical results were not correlated with the EEG findings [the authors considering that the EEG was of limited value in the diagnosis of petit mal].

[In a communication to the British Paediatric Association (*Arch. Dis. Childh.*, 1953, **28**, 243) the abstracter reported that the efficacy of milontin was significantly related to the type of minor seizure. Pure petit mal with a 3-c.p.s spike-and-wave form in the EEG was controlled four times more effectively than the akinetic form in which the EEG showed an atypical spike-and-wave form.] *J. G. Millichap*

NEUROMUSCULAR DISEASES

593. **Some Effect of Extracts of Thymus Glands Removed from Patients with Myasthenia Gravis**
A. WILSON, A. R. OBRIST, and H. WILSON. *Lancet* [*Lancet*] **2**, 368–371, Aug. 22, 1953. 4 figs., 35 refs.

During the past 50 years attention has been given to the possible relationship between the thymus gland and the symptoms of myasthenia gravis. The authors, after reviewing the relevant literature, describe their own investigations at the University of Liverpool.

Thymus glands removed at operation were extracted in acetone; the acetone was then evaporated *in vacuo*, and the fraction suspended in saline and centrifuged. The acetone-insoluble portion was homogenized with saline and centrifuged; the supernatant fluids were combined and the *p*H was adjusted to that of Tyrode solution.

The activity of this preparation was compared with that of D-tubocurarine chloride on the phrenic-nerve–diaphragm preparation of the rat. The muscle was electrically stimulated indirectly, and the contraction recorded by a spring-loaded lever on a drum, the test substance being added to the Tyrode solution in the bath. The thymus glands from 42 patients were thus tested; all the glands were persistent or enlarged, and without tumour. They were divided into three groups according to the clinical effect which their removal had produced, but the identity of these groups was not revealed until after the experiments were completed. It was found that the glands containing the greatest amount of substance inhibiting muscle contraction were from patients in whom there had been the greatest improvement as a result of removal of the glands. In thymus glands removed from adult non-myasthenic patients there was little or no activity, whereas in glands removed from children activity was marked.

The relation of these findings to the causation of myasthenia gravis is the subject of speculation.

G. S. Crockett

594. **The Thyroid Gland in Relation to Neuromuscular Disease**

C. H. MILLIKAN and S. F. HAINES. *Archives of Internal Medicine* [*Arch. intern. Med.*] **92**, 5–39, July, 1953. 8 figs., bibliography.

Writing from the Mayo Clinic, Rochester, Minnesota, the authors discuss the relationship between disorders of the thyroid gland and of muscle innervation under two main heads: (1) thyrotoxicosis in relation to myasthenia gravis, chronic thyrotoxic myopathy, periodic paralysis, and exophthalmic ophthalmoplegia; and (2) hypothyroidism and altered muscle function.

The association between thyrotoxicosis and myasthenia gravis is discussed at some length and 25 case histories are presented. The authors find the incidence of hyperthyroidism before, during, or after the appearance of detectable myasthenia gravis to be only 5%, and they believe the two diseases to be quite separate, without any such reciprocal relationship as others have suggested. In presenting histories of 9 cases of thyrotoxic myopathy they offer suggestions as to how to distinguish this condition from myasthenia gravis. Periodic paralysis (of which 6 reported cases are briefly reviewed) occurs in association with thyrotoxicosis more often than can be explained by chance and it is usually improved by treatment of the thyrotoxicosis. Nevertheless, the authors believe on clinical and laboratory evidence that the two diseases are separate, but suggest that periodic paralysis may be a latent abnormality which becomes manifest in the presence of thyrotoxicosis. Exophthalmic ophthalmoplegia appears to be due to enlargement of the contents of the orbit and very little is known of its cause. The occurrence of severe ophthalmoplegia with very mild exophthalmos indicates that simple stretching of the muscles is not the full explanation of the condition. Exophthalmos has been produced experimentally in animals by administration of extract of anterior lobe of the pituitary, but this has not been confirmed in human subjects.

In hypothyroidism the time of muscle contraction is prolonged as a result of the stretch reflex. Thyroid dysfunction can alter muscle function, and does so apparently through its effect upon muscle metabolism rather than through any effect upon the nervous system controlling the muscles.

G. S. Crockett

595. **Creatine and Guanidoacetic Acid Metabolism in Muscle Disease**

J. N. CUMINGS. *Brain* [*Brain*] **76**, 299–310, 1953. 3 figs., 17 refs.

Further to his previous work on patients with pituitary disease (*J. clin. Path.*, 1950, **5**, 345; *Abstracts of World Medicine*, 1951, **9**, 300) the author now reports a study of creatine and guanidoacetic acid metabolism in 67 patients with various muscle diseases investigated at the National Hospital, Queen Square, London. The patients were on a meatless and fish-free diet for at least 5 days, after which estimations of creatine and creatinine levels in both blood and urine and of the guanidoacetic acid level in the urine were made. A creatine tolerance test was carried out on the 3rd day. In selected cases the blood arginine and guanidoacetic acid values were also measured, and in some other cases a pyruvate metabolism test was carried out. Muscle biopsy specimens were obtained in 13 cases and subjected to chemical analysis. The diagnosis of the muscle disorder was considered, on clinical or histological grounds, to be certain in all cases.

Normal results were found in myotonic congenita, in some cases of myasthenia gravis, and in myopathic ophthalmoplegia. Creatinuria was found in myotonia atrophica and in generalized muscular dystrophy, these being the only two groups that showed a marked diminution of creatine tolerance. Patients with myasthenia gravis from whom it was impossible to withhold neostigmine showed slight creatinuria, but it was difficult to establish a correlation between the severity of the disease and the amount of creatine excreted (one case that proved fatal showed very low creatine excretion). Excretion of creatine was also observed in patients with neuronopathy, dermatomyositis, and porphyrinuria. The excretion of guanidoacetic acid was normal in nearly all cases, but 2 cases of polyneuritis associated with porphyrinuria showed marked creatinuria and also extremely low excretion of guanidoacetic acid.

It is concluded that the tests are of value in cases of difficulty in the clinical diagnosis of a muscular disorder. If the creatine tolerance is reduced so that 40% or more of ingested creatine is excreted, the probable diagnosis lies between myotonia atrophica and myopathy, the latter being the more likely. If there is marked wasting without alteration of creatine tolerance, then neuropathy is indicated, and this is frequently associated (as it was in 50% of the present series) with abnormality of pyruvate metabolism.

Donald McDonald

596. **Progressive Neuropathic (Peroneal) Muscular Atrophy (Charcot–Marie–Tooth Disease). Histological Findings in Muscle Biopsy Specimens in Fourteen Cases, with Notes on Clinical Diagnosis and Familial Occurrence**

A. BRODAL, S. BÖYESEN, and A. G. FRÖVIG. *Archives of Neurology and Psychiatry* [*Arch. Neurol. Psychiat. (Chicago)*] **70**, 1–29, July, 1953. 26 figs., 42 refs.

This paper consists mainly of the results of a study, made at the Neurological Clinic and Anatomical Institute, University of Oslo, of the histology of 20 biopsy specimens of affected muscles from 14 patients suffering from Charcot–Marie–Tooth disease. The changes described are well illustrated in accompanying photomicrographs. The authors found that when the changes were compared with those occurring after peripheral nerve injuries and other muscular atrophies resulting from disease of the lower motor neurone, it was apparent that the muscle changes in progressive neuropathic muscular atrophy are due to a disorder of the motor neurone rather than to a primary muscular disorder. It is concluded that the mode of inheritance of this disease appears to be purely dominant.

J. W. Aldren Turner

Psychiatry

597. **Studies on the Physiology of Awareness. The Interrelationships of Emotions, Life Situations, and Anoxemia in Patients with Bronchial Asthma**
J. W. L. DOUST and D. LEIGH. *Psychosomatic Medicine* [*Psychosom. Med.*] **15**, 292–311, July–Aug., 1953. 5 figs., 41 refs.

The authors have examined, at the Bethlem Royal and Maudsley Hospitals, London, the relationship between emotional tension, arterial oxygen saturation, and asthmatic attacks in 25 patients with bronchial asthma. The deliberate stimulation at interview of anxiety, misery, rage, and other emotions provoked a fall in arterial oxygen saturation to levels as low as 86%. This anoxaemia could be dispelled by the patient giving motor expression to his emotion, by weeping, acting-out of anger, confession, and so forth. It could also be dispelled by simulated asthmatoid breathing, and by an asthmatic attack, which is thus, it is claimed, shown to have a biological function. In some patients an alternative response to the experimental stress was a state resembling primary shock, with the appearance of pallor, sweating, rapid faint pulse, and low blood pressure.

[The asthmatic attack is but one form of reaction to stress. Since anoxaemia appears to accompany all emotional excitement, it seems likely that its relief by the asthmatic attack is not biologically purposeful, but fortuitous.] *Desmond O'Neill*

598. **Insulin Tolerance in Schizophrenia**
G. NADEAU and Y. ROULEAU. *Journal of Clinical and Experimental Psychopathology* [*J. clin. exp. Psychopath.*] **14**, 69–77, April–June, 1953. 4 figs., 21 refs.

In an investigation of glucose metabolism in patients with schizophrenia, insulin tolerance tests were carried out on 46 schizophrenic patients at the Hôpital Saint-Michel-Archange, Mastai, Quebec. In the majority there was a delayed response to 0·1 unit of insulin per kg. body weight, with a tendency to hypoglycaemic unresponsiveness. No correlation was found between the blood sugar level during the test and the subsequent dose of insulin necessary to induce coma; nor was any relationship observed between the degree of hypoglycaemia and the duration of coma. Some patients [number not stated], including 4 who were insulin-resistant, were given 25 g. of glucose 30 minutes before the test was performed. It was found that the response to insulin and to induced hypoglycaemia was normal.

It is suggested that this responsiveness may be due to temporary inactivation of the physiological antagonists to insulin, such as the adrenal and pituitary hormones, and that administration of glucose before the insulin injection in schizophrenic patients who are insulin-resistant might be worth while. The therapeutic possibilities of this are being investigated. *L. G. Kiloh*

599. **Lobotomy and Epilepsy. A Study of 1000 Patients**
W. FREEMAN. *Neurology* [*Neurology*] **3**, 479–494, July, 1953. 15 refs.

In view of the occurrence of convulsive seizures in some 25% of patients after prefrontal lobotomy, an investigation into the factors involved was undertaken at George Washington University, Washington, D.C. Follow-up studies were conducted on 622 patients for 2 to 15 years after prefrontal lobotomy, and the findings compared with those from 498 patients followed up for 1 to 7 years after transorbital lobotomy.

In both groups the lowest incidence of convulsive seizures was found in those patients who had undergone the operation once only, with no complications, and who were free from pre-existing brain disease or epilepsy, whereas the highest incidence was found in those with pre-existing brain disease, operated on two or more times, and who had had operative complications. When patients with a previous history of epilepsy and those in whom operative complications had occurred were excluded from analysis, it still appeared that the presence of pre-existing brain disease or the performance of multiple lobotomy operations greatly increased the liability to seizures, whereas neither previous electric convulsion therapy nor the nature of the mental disorder was a significant factor. On the other hand the incidence of convulsions was somewhat higher in patients under 60 than at a greater age, and in men than in women. Moreover, propinquity of the incision to the motor areas of the cortex was clearly associated with a liability to postoperative seizures, the incidence after prefrontal lobotomy being 24%, whereas that after transorbital lobotomy was only 2%, patients with a past history of fits being excluded in each case.

An interesting finding was that 11 patients who had a history of convulsive seizures before operation became free of them afterwards. However, in only 3 of these cases was there convincing evidence that the lobotomy was directly responsible, the fits in these cases, after occurring fairly frequently up to the time of operation, having then stopped completely for several years. It is suggested that this "paradoxical" relief may be the result of a general improvement in mental and physical health consequent upon lobotomy. *Adrian V. Adams*

600. **Effects of Convulsions Induced by Various Types of Electric Stimulation upon the Cerebrospinal Fluid**
M. SPIEGEL-ADOLF, C. W. UMLAUF, and E. G. SZEKELY. *Journal of Neuropathology and Experimental Neurology* [*J. Neuropath.*] **12**, 363–367, Oct., 1953. 12 refs.

601. **Attempted Suicide in Old Age**
I. R. C. BATCHELOR and M. B. NAPIER. *British Medical Journal* [*Brit. med. J.*] **2**, 1186–1190, Nov. 28, 1953. 8 refs.

Dermatology

602. **Isoniazid in the Treatment of Sarcoidosis. A Preliminary Report**
E. EDELSON. *Journal of Investigative Dermatology* [*J. invest. Derm.*] **21**, 71–74, Aug., 1953. 2 refs.

The results obtained with isoniazid in the treatment of sarcoidosis are described in this paper from Newark Board of Health Clinics, New Jersey. Isoniazid was given by mouth to 6 patients in a daily dose of 1 mg. per kg. body weight for one week or more, and the daily dose then increased to 3 mg. per kg., treatment being continued for about 6 months. Subjective and objective improvement was observed in 4 cases, in 3 of which detectable lesions were confined to the skin. However, histological examination in these cases showed that there had been no material change.

John T. Ingram

603. **Terramycin in the Treatment of Dermatoses. A Report on 1194 Patients**
H. M. ROBINSON, A. SHAPIRO, I. ZELIGMAN, and M. M. COHEN. *Southern Medical Journal* [*Sth. med. J. (Bgham, Ala.)*] **46**, 773–779, Aug., 1953. 24 refs.

At the University of Maryland School of Medicine, Baltimore, an attempt was made to treat with "terramycin" (oxytetracycline) all the various dermatoses usually encountered in a large dermatological clinic, the drug being given in 466 cases by mouth and in 728 cases by local application as a 3% ointment. In the group treated orally the initial dose for all adults of average size was 2 g., followed by 0·5 g. 4 times daily. The drug proved of value in all pyogenic conditions, in erythema multiforme (good results in 17 of 24 cases), and in granuloma inguinale (good results in 10 of 11 cases). It was considered to be of some value in acne vulgaris and acne conglobata, but was not curative, the majority of cases relapsing after the drug was stopped. In secondarily infected eczema, seborrhoeic dermatitis, stasis ulcers, and epidermophytosis it had no beneficial effect on the primary disease. In 4 of 9 cases of herpes zoster there was prompt relief of pain, with disappearance of the lesions in 6 to 12 days, but the course of the disease was unaffected in the remaining 5 cases, in 2 of which severe post-herpetic pain developed which was not benefited by terramycin. Few adverse effects were noted; nausea occurred in 9 cases, nausea and vomiting in 11, diarrhoea in 5, pruritus ani in 2, and vague abdominal pain in one. No blood dyscrasias were noted.

The results of local treatment with 3% terramycin in an ointment base of lanolin and petrolatum were good in all types of pyoderma treated, especially impetigo contagiosa and ecthyma, and the secondary infection was rapidly cleared in eczematous eruptions, epidermophytosis, insect bites, wounds, seborrhoeic dermatitis, stasis ulcers, kerion, and contact dermatitis, though the ointment had no effect on the underlying condition. Eight patients developed a mild contact sensitivity and 3 a severe dermatitis. In all these a positive skin reaction to terramycin powder was obtained, while control patch tests with the ointment base were negative. The ointment proved of no value in the treatment of fungus infections.

The authors conclude that terramycin is a valuable drug in the treatment of skin diseases but that, as with all antibiotics, it should be used only where there is a specific indication. *E. W. Prosser Thomas*

604. **Staphylococcic Ambotoxoid in Treatment of Pustular Acne**
W. L. DOBES. *Southern Medical Journal* [*Sth. med. J. (Bgham, Ala.)*] **46**, 765–769, Aug., 1953. 11 refs.

The pustulation in many cases of acne may be an "id"-like reaction—a manifestation of specific allergic sensitivity due to cutaneous re-exposure or re-inoculation—the organisms in which may be demonstrable only with difficulty or not at all. Specific therapy and prophylaxis should therefore aim at both desensitization to staphylococcal allergens and immunization to staphylococcal toxin. The preparation used by the author incorporates staphylococcal exotoxin in the form of a toxoid with the endotoxic antigenic principles from many different strains of staphylococci lysed by bacteriophage. This "ambotoxoid" was used in treating 34 patients with pustular and cystic acne which had not improved with the usual measures, including autogenous vaccines, the initial dose being 0·1 ml. of a 1-in-10 dilution injected intradermally. The results, which are described by the author as only moderately successful, were: 61% cured or greatly improved, 12% improved, and 26% failed.

E. W. Prosser Thomas

605. **The Age Distribution of Lupus Vulgaris.** (Die Alterdisposition beim Lupus vulgaris)
A. PROPPE and G. WAGNER. *Zeitschrift für Haut- und Geschlechtskrankheiten* [*Z. Haut- u. GeschlKr.*] **14**, 376–381, June 15, 1953. 4 figs., 27 refs.

It has been generally accepted that the age of onset of lupus vulgaris is almost entirely confined to the first two decades of life. In this paper from the University of Kiel the authors analyse the age of onset in 5,789 cases of lupus vulgaris seen in clinics at Düsseldorf and in Niedersachsen and Schleswig-Holstein, and show conclusively that when the number of new cases is compared with the population of the corresponding age group, there is no great difference in incidence of new cases between any of the first seven decades. For example, in the period 1930–39 the average number of new cases per 100,000 of the population in the five decennial age groups from 10 to 60 years was between 1·3 and 1·4, while for the group under 10 years it was 1·16, and for those over 60 years it was 0·9 per 100,000. *H. R. Vickers*

606. **The Growth in the Developing Chicken Embryo of a Filtrable Agent from Verruca Vulgaris**
J. A. BIVINS. *Journal of Investigative Dermatology* [*J. invest. Derm.*] **20**, 471–481, June, 1953. 6 figs., 31 refs.

An agent was obtained from a human wart which caused massive proliferation and "pearl" formation when inoculated on the CAM [chorio-allantoic membrane] of 10-day-old chick embryos. Some virus was present in the liver and allantoic fluid of affected embryos, but it was much more concentrated in the CAM. It was readily filterable through a Berkefeld "V" candle but not at all through a Boerner filter pad. No virus-neutralizing antibodies were demonstrated in the patient's serum. The agent was somewhat susceptible to the action of terramycin [oxytetracycline], aureomycin, and phenyl mercuric nitrate but not to streptomycin.—[Author's summary.]

607. **Ocular Pemphigus**
R. E. CHURCH and I. B. SNEDDON. *British Journal of Dermatology* [*Brit. J. Derm.*] **65**, 235–245, July–Aug., 1953. 5 figs., 23 refs.

The authors consider that ocular pemphigus is a disease entity completely separate from other members of the pemphigus group, and that it never undergoes transition to pemphigus vulgaris. Females are affected more frequently than males, and the onset is generally late in life; in the 7 cases here reported from the Royal Infirmary, Sheffield, 6 of the patients were women, and the average age was 67. The mucosa of the mouth and genitalia may be affected as well as the eyes, and this may occur either before or after the conjunctival involvement. Scaly erythematous patches, with bullae and scarring, occur mainly on the scalp and face. The appearance of discrete bullae on apparently unaffected skin, but near the affected mucosa, is described. Histologically, the bullae can be demonstrated to be situated sub-epidermally, a fact which may be useful in the differential diagnosis from other types of pemphigus.

Treatment, which included the administration of cortisone and of aureomycin and other antibiotics, has proved unsatisfactory. Potassium iodide produced exacerbations in 2 out of 3 cases in which it was given. The prognosis is poor, and although death from the disease is believed to be rare, progression to blindness is to be feared in most cases. *Kate Maunsell*

608. **Ocular Psoriasis. Clinical Review of Eleven Cases and Some Comments on Treatment**
R. KALDECK. *Archives of Dermatology and Syphilology* [*Arch. Derm. Syph. (Chicago)*] **68**, 44–49, July, 1953. 2 figs., 5 refs.

The author, after commenting on the strange lack in textbooks of dermatology of mention of psoriasis affecting the eye, proceeds to describe 11 cases of "psoriasis of the eye" occurring among 90 unselected cases of psoriasis seen in private practice between 1944 and 1952.

[Psoriasis in general is one of the commoner skin diseases, and yet the abstracter has never seen an example of any affection of the eye associated with it, as is quite frequent in rosacea and other skin affections. The description given by the author of the lesions affecting the lid margin and conjunctivae does not convince the abstracter that the condition was other than a blepharitis, and the response of many of the cases to the local application of ointment of yellow oxide of mercury supports this view. It would appear that further observation and investigation is advisable before accepting the diagnosis of ocular psoriasis.]
J. E. M. Wigley

609. **The Treatment of Lupus Erythematosus with Mepacrine and *para*-Aminobenzoic Acid**
H. BLACK. *British Journal of Dermatology* [*Brit. J. Derm.*] **65**, 195–203, June, 1953. 5 refs.

The comparative effects of mepacrine and *para*-aminobenzoic acid (PABA) in the treatment of lupus erythematosus are described in this paper from the General Infirmary at Leeds. The results obtained with mepacrine were definitely superior to those obtained with PABA, improvement being observed in 42 out of 60 patients as against 14 out of 32 who received PABA. The patients who failed to respond to mepacrine also failed to respond to PABA. Mepacrine was more effective in females than in males and in patients without scarring than in those with scarring; no such selective action was observed with PABA. Dosage was not the determining factor in the success or failure of the drug; in some patients the condition cleared up with a dosage of 100 mg. of mepacrine twice daily for only one month, while in others a dosage of 100 mg. 3 times a day for 4 months was necessary; the dosage of PABA varied from 0·5 g. three times a day for 3 months to 1 g. three times a day for 6 months. Skin staining was not a significant factor in those who improved with mepacrine: the skin of a few who did well was only slightly stained or not at all; nor was duration of the disease before treatment a significant factor with either drug.

The only side-effect of any consequence was lichenoid dermatitis, which occurred in 2 patients after a relatively long course of mepacrine. The other side-effects, however, which included generalized itching, nausea, and malaise, might cause the patient to cease taking the tablets. The follow-up period was too short to allow of a firm assessment of the results of treatment; there was a moderate relapse rate, and the author seems doubtful whether mepacrine can be regarded as anything more than another useful drug likely to produce temporary improvement in lupus erythematosus. He believes that part, at least, of its effectiveness is due to a light barrier action. *E. W. Prosser Thomas*

610. **Lupus Erythematosus and Mepacrine. A Fatal Case.** (Lupus érythémateux et atébrine. Un cas de mort)
X. VILANOVA and J. M. DE MORAGAS. *Annales de dermatologie et de syphiligraphie* [*Ann. Derm. Syph. (Paris)*] **80**, 360–362, July–Aug., 1953.

Following the work of Page (*Lancet*, 1951, **2**, 755; *Abstracts of World Medicine*, 1952, **11**, 76) the authors have treated a number of cases of lupus erythematosus with mepacrine with good results. They now report, however, the death of a woman aged 73 who was

given treatment with mepacrine for chronic discoid lupus erythematosus of the face and scalp. The lesions responded rapidly, and after 55 days the disease appeared to be clinically cured, the patient having received a total of 8·1 g. of mepacrine. At this time, however, she became gravely ill with dyspnoea and intense headache, and died 6 days later. Three days before death the blood picture (which had been normal before treatment began) was one of agranulocytosis. No visceral lesions were discovered at necropsy.

According to reports in the literature dealing with the prophylactic use of mepacrine in malaria the development of agranulocytosis is very rare (2·84 cases per 100,000). The authors suggest that the agranulocytosis is probably a sensitization phenomenon rather than a specific toxic effect of meparcrine, and they do not think it necessary, in view of the rarity of grave complications, that mepacrine should be abandoned in the treatment of lupus erythematosus. *James Marshall*

611. **The Surface Skin Fat in Seborrhoeic Dermatitis**
I. S. HODGSON-JONES, R. M. B. MACKENNA, and V. R. WHEATLEY. *British Journal of Dermatology* [*Brit. J. Derm.*] **65**, 246–251, July–Aug., 1953. 2 figs., 6 refs.

The authors report the results of an investigation at St. Bartholomew's Hospital, London, in which they made a comparative study of the amount and composition of the surface skin fat in 20 normal subjects and in 20 patients suffering from seborrhoeic dermatitis. The methods of analysis, after extraction of the surface fat with carbon tetrachloride, are described and the results are tabulated. Quantitatively, there were found to be considerable differences in the fat present in the skin on different parts of the body. The forehead possessed the highest level, followed by the chest, back, and axilla (that is, the areas directly affected in seborrhoeic dermatitis), but there was no significant difference between patients and controls in the average sebum level for most areas.

For the study of the composition of the skin fat, specimens were obtained from the central portion of the back, and the following were determined: (1) the acid number (a measure of the amount of free fatty acid present); (2) the iodine number (a measure of the degree of unsaturation of the fat); (3) the percentage of squalene (unsaponifiable matter); and (4) the percentage of cholesterol. The qualitative results showed that in seborrhoeic dermatitis the iodine number and squalene content were lowered, while the cholesterol content was raised. The acid number was generally normal, but there was a marked alteration in the ratio of cholesterol to squalene.

The authors conclude that in seborrhoeic dermatitis there is an alteration in the composition of sebum as a whole, rather than an excess or deficiency of any one component; but it is not possible to say whether the changes play a causative role, or whether they are the result of a disorder of metabolism, particularly of squalene and cholesterol, caused by the disease process. *Benjamin Schwartz*

612. **Lichen Sclerosus et Atrophicus in Young Subjects**
T. KINDLER. *British Journal of Dermatology* [*Brit. J. Derm.*] **65**, 269–270, July–Aug., 1953. 5 figs., 28 refs.

Lichen sclerosus, especially in its ano-genital manifestations, is reputed to be extremely rare in children. The author therefore reports 8 cases of lichen sclerosus in young girls aged 2 to 13 seen by her in various hospitals in London and observed during the last 3 to 7 years. A brief review of the literature and a description of the clinical picture and histology of the condition is given. The differential diagnosis of cutaneous lichen sclerosus from scleroderma guttatum and lichen planus atrophicus, and of vulval lesions from leucoplakia, kraurosis, scleroderma, and lichen planus is discussed.

Case histories of 3 of the patients are given in detail. In 6 cases the lesions were in the vulva or ano-genital region and in 2 the involvement was solely cutaneous. The skin lesions were symptomless, and in 4 of the ano-genital cases there was discomfort or irritation only in the early stages. The cutaneous lesions in the 2 cases so affected resolved spontaneously when the girls reached puberty, but in the ano-genital cases treatment, which included the local and oral administration of oestrogens, with vitamin A, calciferol, and α-tocopherol, as well as the application of cortisone ointment, proved ineffective. The subjective symptoms here, however, responded to application of an antihistamine cream.

The author believes that lichen sclerosus is not quite so rare in children as is generally assumed, and may frequently be overlooked owing to lack of symptoms. She could trace no aetiological connexion with general diseases or infections, or with psycho-neurological disturbances [although she reports 3 of the patients as being "highly strung"] but suggests that the possible part played by an endocrine factor may be revealed by prolonged observation, to the age of sexual maturity, of these and similar young patients. *Benjamin Schwartz*

613. **Plantar Warts. Cure by Injection**
E. C. BRANSON and R. L. RHEA. *New England Journal of Medicine* [*New Engl. J. Med.*]. **248**, 631–632, April 9, 1953. 1 fig., 5 refs.

A simple and effective treatment for plantar warts, as carried out at the Fifth General Hospital, United States Army, is described. An injection of 2 to 3 ml. of 1% solution of procaine is given under pressure into the plantar wart. The needle is pushed through the normal skin and along the side of the wart until it reaches the stratum germinativum. If the needle is properly placed —that is, not too deep—marked blanching of the skin will occur with elevation of the wart. After a week the softened and darkened wart can usually be lifted out with forceps. *Kate Maunsell*

614. **Aetiology, Pathogenesis, and Treatment of Vitiligo**
(Étiopathogénie et traitement du vitiligo)
F. LEBEUF. *Annales de dermatologie et de syphiligraphie* [*Ann. Derm. Syph.* (*Paris*)] **80**, 363–370, July–Aug., 1953. Bibliography.

Paediatrics

615. **Coeliac Disease—IV. An Investigation into the Injurious Constituents of Wheat in Connection with their Action on Patients with Coeliac Disease.** [In English]
J. H. VAN DE KAMER, H. A. WEIJERS, and W. K. DICKE. *Acta paediatrica* [*Acta paediat. (Uppsala)*] **42**, 223–231, May, 1953. 7 figs., 12 refs.

Previous investigations having shown that wheat flour is harmful in patients with coeliac disease, the authors studied the effect of the constituents of wheat flour on patients at the Wilhelmina Children's Hospital, Utrecht, and the Juliana Children's Hospital, The Hague. Wheat flour was fractionated into gluten, gluten washings, gliadin, and glutenin. It was found that the gluten washings did not cause any deterioration in the condition of the children, but that glutenin, gluten, and gliadin gave rise to considerable steatorrhoea, gliadin being the most potent fraction in this respect. Oatmeal had a deleterious effect on 2 of the patients. *A. C. Frazer*

616 (*a*). **Peptic Ulcer in Childhood**
B. R. GIRDANY. *Pediatrics* [*Pediatrics*] **12**, 56–61, July, 1953. 3 figs., 8 refs.

616 (*b*). **Peptic Ulcers in Children. With Report of Four Cases**
R. C. AYE. *Radiology* [*Radiology*] **61**, 32–38, July, 1953. 9 figs., 25 refs.

The authors of these two papers emphasize that peptic ulceration in childhood is not as infrequent as is sometimes thought. Girdany reports 45 cases seen at the Children's Hospital, Pittsburgh, during a 12-month period, the youngest patient being 14 months of age and the eldest 11 years and the symptoms varying in duration from 3 weeks to 5 years. The clinical histories of these patients were not dissimilar from those of adults with gastric ulcer, namely, pain relieved by food and sometimes by vomiting. In all cases an ulcer crater and deformity of the duodenal bulb were demonstrable radiologically. Treatment consisted in diet, with or without antacids or antispasmodics, and in all patients marked improvement or complete subsidence of pain occurred. The author is of the opinion that emotional disturbances and psychic trauma are often present in children with signs and symptoms of peptic ulcer, and that these may be of major importance in explaining the occurrence of the disease.

Aye, writing from Evanston Hospital (Northwestern University Medical School), Illinois, defines a chronic peptic ulcer as one in which symptoms have been present for 2 months or more, in which a niche is demonstrable radiologically, and where medical treatment has produced partial or complete amelioration of symptoms. He describes 4 such cases, all in boys, one aged 3, two aged 4, and one aged 10 years, and in all of whom an emotional factor was present; in 3 cases the ulcer was duodenal and in 1 case gastric. A table appended gives details of the 45 cases of chronic gastric ulcer in children recorded in the literature since 1843.

Jas. M. Smellie

617. **Acute Appendicitis in Infancy and Early Childhood**
G. L. BUNTON. *British Medical Journal* [*Brit. med. J.*] **2**, 71–73, July 11, 1953. 1 fig., 18 refs.

During 1950–2 appendicectomy was performed on 115 children under 12 at the Westminster Children's Hospital, London, 28 of the patients being under 5. In these younger children the incidence of peritonitis was high (43% as compared with 18% in older children) and upper respiratory infections and diarrhoea were common (18%). The author states that appendicectomy should be carried out promptly, except in the presence of an abscess, which should be treated expectantly, the appendix being removed 6 months later. He prefers Graham's incision to McBurney's, as being quicker to make and close and more easily extended. The recent fall in mortality after appendicectomy is attributed to the use of antibiotics, especially aureomycin, which in the present series was given in doses of 100 mg. 6-hourly in the intravenous drip. There were no deaths.

Discussing the pathology, the author points out that lymphoid tissue in the appendix of young children is abundant and a general infection of lymphoid tissue may involve the appendix (69 of the children had tonsillitis, otitis, or a cold). The appendix being thin-walled and the omentum small, perforation and general peritonitis are consequently common. In the author's view it is dangerous to assume that acute appendicitis is rare in children under 3 years; 22 of his patients were 3 years or less.

The early symptoms of appendicitis are pyrexia, abdominal pain, vomiting, and tenderness, but any of these may be absent; the temperature is often above 101° F. (38·3° C.). Diarrhoea is a frequent symptom, and this the author attributes to the proximity of the appendix to the rectosigmoid in the small pelvis.

Charles P. Nicholas

618. **Acute Intussusception. Analysis of One Hundred and Sixteen Cases at St. Louis Children's Hospital**
D. L. THURSTON, J. HOLOWACH, and E. E. MCCOY. *Archives of Surgery* [*Arch. Surg. (Chicago)*] **67**, 68–79, July, 1953. 1 fig., 14 refs.

In the hope of contributing to present knowledge of the aetiology, diagnosis, and treatment of acute intussusception the authors reviewed 116 consecutive cases seen at the St. Louis Children's Hospital between 1934 and 1951.

There was a marked rise in the incidence of cases during the summer months, suggesting a possible relationship to seasonal diarrhoea, but only in 2 cases

was there a history of diarrhoea immediately before the acute onset of intussusception. Demonstrable primary or contributory organic causes, such as Meckel's diverticulum and adenomata of the ileum, were found more frequently in this series than in other reported series. The classic signs—pain, vomiting, blood in the rectum, and a palpable mass in the abdomen or rectum—were observed in this order of frequency. Shock, though not the most constant, was the most striking symptom observed. [No mention is made of Dance's sign in the diagnosis of the condition.] The authors observed a sharp decline in the mortality in the last 51 cases in this series as compared with 51 cases in a much earlier series. This they attribute to improved surgical technique and pre- and post-operative care rather than to earlier diagnosis.

The observation of Ladd and Gross that the more caudal the intussusceptum the higher the mortality was not confirmed, nor was there any constant relation between duration of symptoms and the distance the intussusceptum had travelled. Spontaneous reduction occurred in a number of cases; in no case in the series was non-surgical reduction attempted. Appendicectomy, when the condition of the patient allowed, was usually performed but other operative procedures, such as bowel fixation, appeared to be inadvisable. The authors state that the value of these procedures in preventing a recurrence is problematical and that the incidence of postoperative adhesions and obstruction, and hence the mortality, are increased thereby.

There were 17 cases (14·6%) of gangrenous bowel in the series, but in none of these was the duration less than 12 hours; in most of them it was more than 48 hours. In this group 8 patients died, a mortality of 47%, whereas in the series as a whole 10 patients died, a mortality of 8·6%. *W. Mestitz*

619. **Association of *Escherichia coli* Serogroup O111 with Two Hospital Outbreaks of Epidemic Diarrhea of the Newborn Infant in New York State during 1947**
E. Neter, R. F. Korns, and R. E. Trussell. *Pediatrics* [*Pediatrics*] **12**, 377–383, Oct., 1953. 43 refs.

620. **Primary Myocardial Disease in Infancy and Childhood**
H. D. Rosenbaum, A. S. Nadas, and E. B. D. Neuhauser. *American Journal of Diseases of Children* [*Amer. J. Dis. Child.*] **86**, 28–44, July, 1953. 6 figs., 41 refs.

In recent years the authors have observed at the Children's Medical Center, Boston, some 45 cases of heart disease in infants and young children which could not be classified either as rheumatic or any known form of congenital heart disease. Features common to all the cases were enlargement of the heart, the presence of electrocardiographic abnormalities, no significant murmurs, and a normal blood pressure, and seemed to point to primary disease of the myocardium. In all 26 of the patients died and necropsy showed that 10 of them had subendocardial sclerosis, 10 had idiopathic myocarditis, 3 had glycogen-storage disease of the heart, 2 had medial necrosis of the coronary arteries, and one had an aberrant left coronary artery. These conditions, along with the clinical criteria for differential diagnosis during life and the value of digitalis in some of these cases, are briefly discussed. *R. S. Illingworth*

621. **Vesical Neck Obstructions in Children**
H. P. McDonald, W. E. Upchurch, and C. E. Sturdevant. *Journal of Urology* [*J. Urol.* (*Baltimore*)] **70**, 94–99, July, 1953. 4 figs., 5 refs.

The authors call attention to congenital bladder-neck obstruction—which they consider to be much more common than is generally realized—as a likely cause of recurrent pyuria, pyelitis, enuresis, frequency, urgency, or restricted urinary stream in children. Early recognition is essential in severe cases to prevent or minimize damage to the upper urinary tract. The less severe obstructions may be the forerunners of the obstructive lesions seen at the bladder neck in young adult males. Of 112 children with bladder symptoms who were examined by the authors during a 10-year period, a mass or hypertrophy was found at the vesical neck in 27 and contracture or bar in 17, 14 had a valve-like formation in the deep urethra, 2 had hypertrophy of the verumontanum, 57 had a narrow urethral meatus, and 42 had stricture of the urethra. In many cases multiple obstructions were present.

Patients with mild obstruction may have little or no residual urine and little or no dilatation of the upper urinary tract, while renal function is usually normal. Cysto-urethroscopy shows moderate trabeculation of the bladder, with hyperaemic masses at the vesical neck. Treatment consists in fulguration of the masses through a miniature cystoscope or panendoscope, for which purpose in boys a perineal urethrotomy is often necessary, especially if there is congenital narrowing of the urethra. Fulguration is carried out in two or more stages at 8-week intervals. Meatotomy and urethral dilatation are performed as indicated, together with dilatation of the bladder under general anaesthesia when capacity is subnormal.

Patients with moderate obstruction may have a small amount of residual urine, with moderate dilatation of the upper urinary tract and some damage to the renal parenchyma. Bladder trabeculation is more marked, and larger hypertrophic masses or definite contractures are seen at the bladder neck. In these cases transurethral resection with an infant resectoscope is preferred to fulguration, which may be followed by secondary haemorrhage or delayed healing.

Patients with severe obstruction have marked bladder trabeculation and much residual urine. There is dilatation of the ureters and renal pelves, together with considerable damage to the renal parenchyma, much of which is permanent. In this group preliminary suprapubic cystostomy should be performed to allow maximum recovery of renal function and control of infection. (This may take several years, and in one case suprapubic drainage was maintained for 8 years.) The obstruction is then removed by transurethral resection or open operation. *H. McComb*

Public Health

622. **Tuberculosis Epidemics in Schools.** (Tuberkuloseepidemien in Schulen)
M. DAELEN. *Tuberkulosearzt* [*Tuberkulosearzt*] **7**, 445–452, Aug., 1953. 19 refs.

The author discusses six epidemics occurring in schools in Hesse, Germany, during the years 1948 to 1952, in which 112 children developed active tuberculosis.

In one school, 45 children were infected by a sputum-positive teacher who on radiological examination had been declared free of the disease 2 years previously. In another school an apparently sputum-negative teacher had infected 18 children, but 6 other children who had had B.C.G. vaccination remained healthy. In a third a teacher failed to divulge the nature of her employment to the health authorities, and of her illness to the education authorities; by the time these were revealed, 6 children had been infected. Another teacher had omitted to attend for the routine 3-yearly *x*-ray examination; within 2 years the positive-Mantoux rate in the school had risen significantly from 25 to 72%, and the teacher's own 2 children had converted; 10 children developed active tuberculosis. In another school, infection spread from a child whose parents had refused treatment and had allowed the child to continue to attend school. In the sixth epidemic 47 of 51 children (92%) in one class reacted positively and 23 of them (2 of whom had previously received B.C.G. vaccination) developed active disease before an apparently healthy teacher was found to be suffering from active, progressive, cavitated, sputum-positive tuberculosis.

The author recommends that the compulsory *x*-ray examination of teachers on establishment should be extended to all school staff, including cleaners and porters, and repeated annually, and also that skin testing and B.C.G. vaccination of school-children should be undertaken intensively. Various suggestions for tightening up notification regulations and for better cooperation between the authorities concerned are offered.

E. V. Saunders-Jacobs

623. **Development of Neutralizing Antibodies against the Three Types of Poliomyelitis Virus during an Epidemic Period. The Ratio of Inapparent Infection to Clinical Poliomyelitis**
J. L. MELNICK and N. LEDINKO. *American Journal of Hygiene* [*Amer. J. Hyg.*] **58**, 207–222, Sept., 1953. 4 figs., 30 refs.

The demonstration of specific neutralizing antibodies to all three types of poliomyelitis virus and the development of tissue-culture technique enabled the present authors to undertake a serological survey of the juvenile population of Winston-Salem, North Carolina, during an epidemic in 1948.

Figures are given for the incidence of antibodies to Type-1, Type-2, and Type-3 poliomyelitis virus in the pre-epidemic and post-epidemic periods in various age groups, ranging from the newborn to children of 14 years; for the change in antibody pattern during the poliomyelitis epidemic; for the incidence of multiple antibodies in the same individual; and for the ratio of subclinical infection to clinical poliomyelitis.

During the epidemic Type-1 and Type-2 antibodies were acquired, with infection rates of 23% and 17%. They were found more frequently in children under the age of 4 years than in those over this age. No child developed Type-3 antibody during this investigation. The number of subclinical infections per case of poliomyelitis varied between 175 for infants under 1 year and 62 for children of 6 to 9 years. Previous infection did not prevent the development of other types of neutralizing antibody.

Antibodies to all 3 types of poliomyelitis virus were present to a significantly greater degree in children from lower socio-economic groups, both in pre-epidemic and post-epidemic periods; in this group also Type-1 antibodies developed more readily.

[Those interested should refer to this important article for the detailed results of the serological survey.]

D. Geraint James

624. **Passive Immunization in Relation to Multiple Cases of Poliomyelitis in the Household. Epidemiologic Aspects in New York City, 1949–1952**
M. SIEGEL and M. GREENBERG. *New England Journal of Medicine* [*New Engl. J. Med.*] **249**, 171–177, July 30, 1953. 29 refs.

This analysis of cases of poliomyelitis reported to the Health Department of New York City during the period 1949–52 was made in order to obtain data for the effective application of passive immunization with gamma globulin. Clinical and epidemiological data were obtained by medical inspectors soon after notification. For the clinical diagnosis of poliomyelitis the minimum requirements were fever, stiff neck or back, increased cell count in the cerebrospinal fluid, with or without muscular weakness or paralysis. Between 20 and 25% of reported cases did not satisfy these criteria and were excluded. During the period mentioned, 4,886 cases were reported, in 61% of which there was weakness or paralysis, the mortality, mostly due to bulbar paralysis, being 6%. There were no deaths in the non-paralytic cases. The highest incidence rates were in the age group 5–9. Data on family contacts were obtained in 4,708 cases; more than one case occurred in 167 households, 158 having 2 cases, 7 having 3 cases, and 2 having 4 cases each.

The incidence of single cases in the population at risk ranged in different years from 33 to 94·7 per 100,000 households and multiple cases from 0·8 to 4·4 per 100,000 households. Multiple cases occurred in 4·4%

of affected families in 1949 (an epidemic year) and in 2·4 to 3·0% in the other years, the rate varying directly with the annual incidence of the disease and the age composition of the family: for example, the rate of multiple cases per 100,000 households increased tenfold as the number of children under 18 years of age increased from 0 to 2 or more.

In the 1949 epidemic, of 10,536 persons in the households where infection occurred, 2,338 (22·2%) were affected initially and 108 (1·3%) subsequently, the highest incidence of initial and subsequent infection occurring in the age group 5–9 years. The incidence of subsequent cases in affected households was about 40 times that in the general population. Analysis of age distribution showed that the greatest risk of clinical infection after household exposure occurred in the age period 15–34 years.

About 95% of the secondary cases occurred within 14 days of the initial case, 63% within 7 days, and 52% within 5 days; no case occurred after 31 days. The incidence of subsequent infection after the first week was greater in the older age groups than in the younger, and in 1949 the death rate was twice as high in the age group 15–34 as it was in those under the age of 15, the mortality being independent of the time of onset in the household.

The authors suggest that these results show that, to be effective, gammaglobulin must be given to all household contacts, at least up to the age of 34, as soon as possible after diagnosis of the first case, the time factor being of great importance. As a single dose confers protection for 5 weeks, re-inoculation is unnecessary.

M. Lubran

625. **Epidemic Poliomyelitis and its Prevention**
M. AGERHOLM. *Lancet* [*Lancet*] **2**, 287–293, Aug. 8, 1953. 3 figs., 41 refs.

In this paper from the Nuffield Orthopaedic Centre, Oxford, it is postulated that the serious epidemics of poliomyelitis which have occurred in Great Britain since 1947 are due to the introduction of a strain of virus distinct from that responsible for the endemic form of the disease known here for many years. In the author's view the main factor favouring spread of this virus in a population devoid of herd immunity is personal contact, and she points out that evidence for this mode of infection is likely to be obscured by the occurrence of infection which is too slight to be diagnosed. In support of this contention she discusses a local outbreak in the Isle of Wight in 1950, where the chain of infection could be traced without difficulty. A period of enforced quarantine of about 2 weeks for all contacts of the primary case would have prevented at least 19 of the 35 cases which arose.

[The author strongly advocates much stricter quarantine regulations for poliomyelitis contacts, though she does not put forward any very practicable scheme for this. To place visitors to an infants' school in the south-west corner of the Isle of Wight in quarantine is one thing, but when individuals in, say, Kent, Surrey, and Middlesex may be regarded as random contacts the problem is very different. Furthermore, the herding together of considerable numbers of poliomyelitis contacts might give rise to at least as many fresh paralytic cases as it would prevent, with no obvious gain to the community; since strict isolation of all contacts from one another and from the outside world is obviously not practicable.]

Joseph Ellison

626. **An Outbreak of Trichiniasis in Barry, Glamorgan. Improved Technique for Demonstration of *Trichinella* in Muscle**
A. D. EVANS and M. LENNOX. *British Medical Journal* [*Brit. med. J.*] **2**, 131–133, July 18, 1953. 3 refs.

The clinical and laboratory findings in 25 cases of trichiniasis in Barry, Glamorganshire, are reported. The patients became ill, after eating pork sausage meat, with typical symptoms of trichiniasis, of which periorbital oedema was the most characteristic. In 20 patients there was an eosinophilia of 10% or over within 7 days of the onset. The incubation period ranged from 11 to 27 days; in 14 patients the first symptoms were observed between the 15th and 24th days, the duration of the symptoms being 4 to 9 weeks. Skin tests with *Trichinella* antigen were carried out on 12 patients; a positive reaction was obtained in 9 cases, a delayed reaction in 2, and a negative response in one.

Larvae of *T. spiralis* were found in rats and in 4 out of 288 diaphragms of pigs from West Pembrokeshire, whence the infected meat had come, but none was found in pigs from the area of Glamorgan which usually supplied Barry.

The authors suggest an improved technique for the demonstration of *Trichinella* in muscle; in this, use is made of both peptic and tryptic digestion of the muscle fibres, the larvae being left still motile. The advantages of this method are the absence of muscle fibres, the greater number of trichinellae recovered, and the preservation of their motility.

Franz Heimann

627. **Infective Hepatitis: a Discussion on its Mode of Spread in Families**
D. J. R. SNOW. *Medical Journal of Australia* [*Med. J. Aust.*] **2**, 139–142, July 25, 1953. 6 figs., 3 refs.

This study of the mode of spread of infective hepatitis within families is based upon observations made during an epidemic in Perth, Western Australia. Among 1,000 cases recorded, 79 were drawn from 31 families in which 2 or more members were affected, including 2 in which all 7 members were affected and another in which all 5 children were affected although the parents escaped. The time-relations of the individual attacks and the probable sequence of infection in these three families are shown diagrammatically, and the various factors affecting the spread of the disease within families are discussed in detail.

The author concludes that the communicability of infective hepatitis appears to be low, and that close and intimate contact seems to be necessary for its transmission. The infective agent is probably conveyed from person to person in faecal particles rather than by the droplet mechanism.

D. Geraint James

Industrial Medicine and Toxicology

628. **Bronchial Carcinoma in Dusty Occupations. Observations in Boiler Scalers and Grain Dockers**
L. DUNNER and M. S. HICKS. *British Journal of Tuberculosis and Diseases of the Chest* [*Brit. J. Tuberc.*] **47**, 145–149, July, 1953. 10 refs.

It would appear, if statistics are to be believed, that the incidence of bronchial carcinoma is higher in patients suffering from asbestosis, siderosis, and the effects of chrome inhalation than in controls, whereas the incidence in patients suffering from silicosis is no higher. Pneumoconiosis occurs in dockers handling grain and in boiler scalers, and the present authors, from the Chest Clinic, Hull, describe 26 cases of bronchial carcinoma occurring in men working in these trades. Of the 26 patients (20 of whom were grain dockers), 14 were seen in 1951–2, a period when the number of deaths from bronchial carcinoma among the general population of Hull was on the increase. There are 5,000 dockers in Hull and only half of these are exposed to dusts; among the other half, and this is probably significant, not one case of bronchial carcinoma was seen. The authors believe that exposure to dust is an aetiological factor, but they admit that the unknown factor responsible for the increased incidence in the general population also played some part. In 5 of their patients there was histological evidence of pneumoconiosis but only in one (a boiler scaler with obvious silicosis) was there radiological evidence of this condition. There were no non-smokers or heavy smokers among their patients. *Paul B. Woolley*

629. **Farmer's Lung**
T. C. STUDDERT. *British Medical Journal* [*Brit. med. J.*] **1**, 1305–1309, June 13, 1953. 2 figs., 19 refs.

Writing from the Cumberland Infirmary, Carlisle, the author discusses the natural history of the condition conveniently termed "farmer's lung", and briefly reviews the literature. The symptoms of this disorder are breathlessness, cough, cyanosis, and slight pyrexia, accompanied by the presence of widespread crepitations in the lungs, and they make their appearance soon after exposure to the dust of mouldy hay. The *x*-ray appearances show increased lung markings, with additional soft shadowing. Spontaneous recovery is usual in about 2 months, but there may be residual emphysema in some cases. It is reputed among farmers occasionally to have caused sudden death, and also to be the cause of broken-windedness in horses. An inquiry showed that most rural doctors are familiar with the disease, especially in north-west England where it is common, but as it usually resolves spontaneously, cases are not often seen in hospital.

In the discussion of aetiology and differential diagnosis, distinction is made between farmer's lung and asthma caused by mouldy-hay dust; the former condition usually develops within 24 hours of exposure and presents as a mild acute pulmonary oedema without cardiac distress. Rigor and vomiting are common at the onset. Recovery from the condition, both clinically and radiologically, is gradual, and may take up to 3 months. In some of the author's cases moulds were isolated from the sputum and often corresponded with those found in the hay dust, but they were not thought to be specifically causal; nor were specific skin-sensitivity reactions to them obtained, as was the case in a patient whose symptoms were those of asthma following exposure to mouldy hay. Consolidation, pleurisy, and haemoptysis do not occur, and these serve to distinguish pneumonia from farmer's lung. Aspergillosis is distinguished by the occurrence of dense infiltration and cavitation, and by the presence of actively growing mould in the sputum.

The condition is considered to be a non-specific reaction of the lung to a variety of irritants, and the similarity of the disease to certain other occupational diseases (for example, coniosporiosis, weaver's cough, byssinosis, and diffuse granulomatous pneumonitis) is stressed. A series of 6 personal cases are described.
L. W. Hale

630. **The Morphology and Pathogenesis of Pumice Pneumoconiosis.** (Morfologia e patogenesi delle pneumosclerosi da pomice)
A. FERRARA and G. FARAONE. *Rivista degli infortuni e delle malattie professionali* [*Riv. Infort. Mal. prof.*] **40**, 453–467, 1953. 10 figs., 13 refs.

This is a general account of the pathology and histology of pneumoconiosis due to pumice dust, based on the post-mortem findings in 4 cases, which are not individually described. The middle zones of both lungs were mainly affected, the apices escaping as a rule. Two types of macroscopic appearance were found—a linear fibrosis, corresponding to the radiological "reticulation", and a massive fibrosis. Unlike other forms of silicosis, the stage of nodulation seems to be entirely absent; the author considers that this may be associated with the low content of free silica (1·85%) in pumice dust. This may also account for the long latent period, perhaps 20 to 30 years, before symptoms develop. Tuberculosis was not found in association with pumice-dust silicosis. Pleural fibrosis was usually present, and also marked enlargement of the mediastinal lymph nodes, but there was no evidence of bronchiectasis, although there was generalized emphysema.

Histologically, the condition did not seem to differ greatly from other forms of silicosis; widespread connective-tissue thickening interspersed with mineral deposits and without extensive cellular infiltration was characteristic. There was no focal emphysema. The bronchial mucosa was greatly swollen and infiltrated with masses of cells and phagocytes containing mineral particles; a true obliterating granulomatous bronchitis was present. Local circulatory obstruction appears to lead eventually to extensive small arterio-venous shunts, and this phenomenon may explain the pulmonary venous

congestion and deficient oxygenation characteristic of silicosis. Pumice dust, containing little free silica, does not quickly set up a local irritant process, but is drained into the lymph nodes and blood stream, with involvement of other organs, including the pleura, and alteration in the blood plasma (dysproteinaemia). Massive fibrosis is not considered to follow bronchial obstruction, but to be due to the arterio-venous lesions already mentioned.

L. G. Norman

631. **A Note on Extrapulmonary Histology in Pumice Worker's Disease.** (Note istologiche extra-polmonari nella malattia silicotica dei lavoratori della pomice)
A. FERRARA and G. FARAONE. *Rivista degli infortuni e delle malattie professionali* [*Riv. Infort. Mal. prof.*] **40**, 468–474, 1953. 5 figs., 21 refs.

Silicosis due to pumice dust affects organs other than the lung, the multi-visceral involvement which occurs justifying, in the authors' opinion, the designation "silicotic disease". Histological changes found post mortem in the liver, spleen, and kidneys in 4 cases are described. The liver showed a diffuse reticulo-endothelial hyperplasia; there were widespread and abundant deposits of a microcrystalline mineral, mainly concentrated in the histiocytes of the portal spaces and the Kupffer cells. The authors consider that the dust is carried to the liver and deposited in crystalline form throughout the process. In one case there was also a diffuse amyloidosis. There was moderate enlargement of the spleen, with hyperplasia of the reticular elements of the pulp, reduction in the number of follicles, and a moderate degree of congestion. Deposits of microcrystalline siliceous material were present, while numerous small infarcts were observed in one of the 4 cases. There was no siderosis. The kidneys showed a widespread deposit of microcrystalline material, less marked than in the liver and spleen, lying mainly in the capillaries of the glomeruli and cortical connective tissue. There was also an early generalized fibrosis, particularly of the glomerular vascular network, with congestion and cellular deposits in and around the tubules. These last changes were probably associated with alteration in the blood protein levels, mainly due to abnormal excretion of serum albumin.

L. G. Norman

632. **Silicosis in the Pumice Workers of Canneto-Lipari in the Light of Recent Scientific Progress.** (La silicosi nei lavoratori della pomice di Canneto-Lipari, sotto il profilo delle recenti acquisizioni scientifiche)
G. FARAONE. *Rivista degli infortuni e delle malattie professionali* [*Riv. Infort. Mal. prof.*] **40**, 194–239, 1953. Bibliography.

From Canneto in the Lipari Islands, which lie between Sicily and Italy "pumice stone", drilled out of the volcanic rock, is exported all over the world. A full chemical analysis of the stone before and after polishing is given; the total silica content varies from 65 to 75%, that of free silica from 1 to 2%. Much dust arises in the processes of extraction and transport, but the greatest quantities are produced during the drying and sifting of the powdered stone. [Particle numbers and sizes are not recorded.] Danger arises not only to the workers but also to the local inhabitants, who extract the stone privately.

In this paper from the University of Messina, a summary is given of the studies of silicosis in this industry which have been made since 1922, together with a good general account of recent advances in the knowledge of silicosis. Post-mortem findings in 2 cases are described, with the histological and mineralogical findings; these are similar to those found in silicosis due to other dusts. A clinical examination of 31 cases resulted in such findings as pulmonary fibrosis, emphysema, cor pulmonale, and "cardio-aortic involvement" [but unfortunately the number of cases showing these signs is not recorded]. Attempts to assess cardio-respiratory function, mainly by spirometry, were unsuccessful owing to variability of the results. The radiographic findings are reported elsewhere [see Abstract 634]. No cases of tuberculosis were found. Electrocardiographic findings are briefly reported. Serological studies suggested that an increase in the serum gamma-globulin fraction was associated with a quiescent fibrosis while an increase in the beta-globulin fraction was present in more active cases, but the number of cases was too small for this to be determined with any certainty.

A full account is given of the medico-legal aspects of assessment in cases of silicosis, from three points of view —diagnosis, determination of the nature of the causative material, and estimation of the amount of damage to the individual (including calculation of the percentage of disability).

[The author has succeeded in his main object, which was to draw attention to the dangers of silicosis in this industry. There is, however, little in this paper which will be new to those who are familiar with silicosis.]

L. G. Norman

633. **Pneumoconiosis due to Pumice Powder. A Clinical and Radiological Investigation in the Pumice Industry of Canneto-Lipari.** (La pneumoconiosi da polvere di pomice. Controllo clinico e schermografico nella industria per la estrazione e la lavorazione della pomice di Canneto-Lipari)
D. COLUMBA. *Rivista degli infortuni e delle malattie professionali* [*Riv. Infort. Mal. prof.*] **40**, 240–271, 1953. 25 figs., bibliography.

This paper reports the results of a clinical and radiological inquiry, carried out by the Italian National Institute for the Prevention of Industrial Accidents, into the incidence of silicosis in workers in the pumice-stone industry of Canneto in the Lipari Islands, and in the other inhabitants. Some figures of the incidence of silicosis throughout Italy, based on national insurance statistics, are first quoted. An account is then given of the method of extraction of pumice and details of the different types of work involved, the annual output being between 60,000 and 65,000 metric tons. With much difficulty, owing to shortage of water and electricity in this backward region, a mass radiography unit [details of which are not given] was set up and 1,061 people were examined, comprising 804 workers in the industry and 257 other inhabitants, large films being taken where any

abnormality was found in the miniature. (A number of typical films are reproduced.) In addition, a general clinical examination was undertaken in all cases.

In only 58% of those examined were the findings in the respiratory system normal, whereas abnormalities in the cardiovascular and other systems were infrequent. Of 804 workers radiographed, the films of 33 showed reticulation, 21 nodulation, 13 massive fibrosis, and one silico-tuberculosis. In addition, 2 active and 6 inactive cases of tuberculosis without any evidence of silicosis were found. Among 257 inhabitants of the same area not employed in the industry, there were 3 cases of reticulation, 2 of nodulation, and none of massive fibrosis or silico-tuberculosis. Two inactive cases of tuberculosis only were found in this group. A full account, with histological findings, is given of one case in which death occurred from massive fibrosis during the period of the inquiry. It is concluded that pumice powder causes a true silicosis in which silico-tuberculosis rarely occurs, and that massive fibrosis does not appear to be associated with the added infection of tuberculosis. The condition is slowly progressive and does not cause serious incapacity except in the most advanced cases. Massive fibrosis is relatively frequent and is thought to be associated with the enormous quantities of dust inhaled. The most severe cases were found in workers who were engaged in sifting the pumice powder, 34% of the particles of which were found to be less than 1μ in diameter; in these workers total incapacity or death after 15 years' exposure appears to be the rule. Preventive measures are discussed; dust-suppression does not appear to be practicable at present. *L. G. Norman*

634. **The Radiological Appearances in Pumice Pneumoconiosis (Liparosis) and their Pathogenetic Interpretation.** (L'aspetto radiologico della pneumoconiosi da pomice (liparosi) e la sua interpretazione patogenetica)
E. CASTRONOVO. *Rivista degli infortuni e delle malattie professionali* [*Riv. Infort. Mal. prof.*] **40**, 278–317, 1953. 56 figs., 40 refs.

During 1951 about 1,200 miniature radiographs were taken of workers and inhabitants in the pumice-quarrying regions of the Lipari Islands [see Abstract 633], and on the basis of his experience in their interpretation the present author discusses the relation between the radiological appearance and the underlying pathological process and its development. In the literature 4 types of pneumoconiosis are distinguished, which the author describes as: (1) inert pneumoconiosis, as in anthracosis; (2) allergic pneumoconiosis, for example, bagassosis; (3) radioactive pneumoconiosis, which has not yet been sufficiently studied and is perhaps more common than is at present supposed; and (4) pneumoconiosis produced by irritant dusts capable of causing a dysproteinaemia. Mixed forms also occur. The author considers the type of silicosis due to pumice dust to differ sufficiently from these 4 types as to justify its designation as a separate type, which he names " liparosis ".

This differentiation is based on a number of factors, the chief one being an apparent absence of nodulation. Generalized severe emphysema was found radiologically in the early cases, preceding the development of reticular shadows, and was the only sign present during the first 10 to 15 years of exposure. These cases progress to reticulation and then to massive fibrosis without any evidence of nodulation. There were no cases of tuberculosis, and tomograms, which were taken in a number of cases, did not reveal any cavitation or zones of necrosis. Well-marked cardiovascular changes were present in the more advanced cases, and consisted mainly of unfolding of the aorta and enlargement of the great veins with subsequent development of cor pulmonale, which is regularly found in fatal cases. These changes may possibly be associated with the ingestion of large quantities of pumice-dust through the alimentary tract. If there is a history of exposure, the author considers the following three signs to be diagnostic of " liparosis "—diffuse emphysema, accentuation of the hilar and basal pulmonary vessels, and atherosclerosis of the aorta. The paper is illustrated by 56 well-reproduced radiographs, mainly miniatures. *L. G. Norman*

635. **Hop Dermatitis in Herefordshire**
J. S. COOKSON and A. LAWTON. *British Medical Journal* [*Brit. med. J.*] **2**, 376–379, Aug. 15, 1953. 11 refs.

An investigation into the incidence of hop dermatitis among workers in hop-yards in Herefordshire in 1952 revealed that one in every 30 pickers had some form of dermatitis. Severe dermatitis was, however, rare, and was associated with oedema of the face and hands and exposed parts. The incidence of this severe form was probably no higher than 1 in 3,000 pickers.

In some cases the dermatitis appeared to be due to a sensitizing ingredient of the hop-oil, which, however, was lost in the process of drying, thus accounting for the rarity of hop dermatitis among workers in dried hops. In some cases a positive reaction to hop resin was obtained. *John T. Ingram*

636. **Side-effects and Sequelae of the Chronic Abuse of Phenacetin.** (Nebenerscheinungen und Folgen des chronischen Phenacetinabusus)
F. SCHAUB, A. BÜHLMANN, and C. MAIER. *Schweizerische medizinische Wochenschrift* [*Schweiz. med. Wschr.*] **83**, 626–629, July 4, 1953. 2 figs., 12 refs.

At the University Polyclinic, Zürich, a study was made of the abnormalities found in the blood of 24 patients, most of them neurotic women, who had been taking excessive amounts of phenacetin in proprietary analgesic preparations. (Some admitted taking about 12,000 tablets, each containing 0·25 g. of phenacetin, a year.) The clinical picture was of greyish cyanosis, with moderate anaemia, usually macrocytic and hyperchromic, and reticulocytosis. The bone marrow showed increased erythropoiesis. The amount of inactive haemoglobin was increased and there was sulphaemoglobin in the blood. In severe cases the oxygen saturation of the arterial blood was subnormal and the oxygen dissociation curve shifted to the right. Predisposing factors, such as iron deficiency and constipation, were common. There was evidence that phenacetin has a direct toxic action on erythropoiesis. *G. V. R. Born*

Anaesthetics

637. **The Acute Hypoxic Episode**
M. S. SADOVE, G. M. WYANT, and L. A. GITTELSON. *British Medical Journal* [*Brit. med. J.*] **2**, 255–257, Aug. 1, 1953. 6 refs.

Haldane has stated that " anoxia not only stops the machine, but wrecks the machinery ". It is pointed out in this paper from the Veterans Administration Hospital, Hines, Illinois, that the surgeon meets hypoxia in its most dramatic form—that is, as acute cardiac failure, arrest, or standstill, and that efficient manual systole must be accomplished within 4 minutes or, if chronic hypoxia preceded the acute episode, in less than 4 minutes. More can be done for the treatment of post-hypoxia than is usually thought to be the case. Total destruction of nervous elements is irreversible, but the authors believe that this is often of minor extent only and that there are large areas of tissue in which the damage is reversible.

One of the sequelae of hypoxia is cerebral oedema, which interposes a physical barrier between the capillaries and the cells; it also raises the intracranial pressure and thus further interferes with the circulation. This is a vicious circle which must be broken. The pre-terminal hyperpyrexia which is often seen in these cases may be explained on the basis of oedema of the heat-regulating centre. Though this sign often precedes death, it need not necessarily do so; the authors consider it to mean only that extensive damage is present which is extending into the hypothalamus.

The authors subject patients who have had an acute attack of hypoxia to a regimen of vigorous dehydration. A case is described of cardiac arrest following prolonged severe anoxia during a thoracic operation. Half an hour after the circulation was restored 50 ml. of 50% glucose was given intravenously, and the coma lightened. Later 1,000 ml. of 25% glucose was given by slow intravenous drip. The patient recovered uneventfully from what might have been a fatal hypoxia. The glucose lightened the coma on each occasion and checked the hyperpyrexia. It is considered that concentrated human serum albumin or concentrated plasma is worth a trial in these cases. Plasma expanders such as dextran are indicated on theoretical grounds. Oxygen is given throughout the post-hypoxic period and a clear airway constantly maintained, secretion often being aspirated through an endotracheal tube. A head-down tilt of the bed at about 7 degrees is helpful. Tracheotomy should be performed if coma is prolonged, and adequate ventilation ensured, if necessary, by the use of a Drinker respirator. Analeptics are not thought to have any place in the treatment of post-hypoxic respiratory depression.

Gastric dilatation is treated by the passage of a stomach tube. To maintain blood pressure, vasopressor drugs are preferred to intravenous administration of fluids over and above the minimum requirements. Antibiotics are given and the patient is turned frequently from one side to the other. Inhalation of carbon dioxide for short periods may also be required. The authors emphasize that the patient must never be left flat on his back for any length of time. To increase cerebral circulation stellate ganglion block, if necessary bilateral, may be employed. *W. Stanley Sykes*

638. **Observation on the Pathogenesis of Laryngeal Granuloma due to Endotracheal Anesthesia**
R. T. BARTON. *New England Journal of Medicine* [*New Engl. J. Med.*] **248**, 1097–1099, June 25, 1953. 4 figs., 4 refs.

The author describes 4 cases, seen at the Veterans Administration Center, Los Angeles, in which, following endotracheal anaesthesia in the face-down position, a pedunculated granulomatous polyp developed on the vocal process of the arytenoid cartilage. In 2 cases the polyp was removed at operation; in a third, in which there had been an antecedent throat infection, the condition cleared up in response to administration of " terramycin " (oxytetracycline) and to resting the voice.

In the fourth case, during removal under local analgesia of a tracheal neoplasm through a midline incision with a bronchoscope *in situ*, it was observed that the bronchoscope lay against the anterior commissure owing to hyperextension of the head on the neck. Later in the operation general anaesthesia was given through a flexible endotracheal tube, which was seen to lie embraced by the vocal processes of the arytenoid cartilages and the posterior commissure. It is suggested that an endotracheal tube usually lies in this posterior location, especially when the head is flexed during operation, and that friction denudes the epithelium, giving rise to an ulcer which subsequently granulates too profusely, so that a polyp is formed.

A plea is made for atraumatic introduction of the endotracheal tube, minimum movement of the neck thereafter, and careful aseptic technique, followed by antibiotic therapy. *Donald V. Bateman*

639. **Controlled Hypotension with Arfonad in Neurosurgery. With Special Reference to Vascular Lesions**
S. ANDERSON and W. MCKISSOCK. *Lancet* [*Lancet*] **2**, 754–757, Oct. 10, 1953. 3 figs., 8 refs.

Recently developed methods of inducing controlled hypotension have very materially widened the scope of neurosurgical intervention, but for certain procedures the methonium compounds, hitherto mainly used, do not give sufficient control over the blood pressure, although this control can be increased to some extent by the addition of procainamide. " Arfonad ", a thiophanium derivative (Ro2-2222), is a rapidly acting vasodepressor drug with ganglion-blocking and direct vasodilator activity. In this paper from St. George's

Hospital, London, the authors report their experience with the drug in the performance of 52 craniotomies. There were 17 cases of vascular abnormality, 22 cases of cerebral tumour, and 13 miscellaneous cases.

Intubation was carried out after induction with thiopentone and a relaxant, anaesthesia thereafter being maintained with nitrous oxide–oxygen, and more relaxant being added to control coughing if required. After positioning the patient on the table, the blood pressure was taken and the table then tilted 25 to 30 degrees in a reverse Trendelenburg position. The blood pressure was again taken 2 minutes later (this is an important basic observation since it provides a valuable guide to the amount of drug required. The arfonad drip was then begun, slowly at first to test the reactions, and the rate eventually adjusted to maintain a systolic pressure of 80 mm. Hg. After opening the dura the pressure was lowered still further, to 60 to 70 mm. Hg, in order to reduce intracranial tension, and this pressure was maintained unless a further decrease was required by the surgeon. Before closing the dura the blood pressure was allowed to return to near normal or to at least 100 mm. Hg by stopping the drip and levelling the table, thus allowing bleeding points to be controlled and lessening the risk of postoperative clot. After replacement of the bone flap, the blood pressure is again reduced to 80 mm. Hg to prevent blood loss from the skin flaps.

Only 2 of the 52 cases required transfusion because of blood loss. No case of postoperative clot was encountered in the last 30 cases since the introduction of the technique described. There were 4 deaths, but all 4 patients were bad risks and death was not attributable to the hypotension. In only one case was the bloodlessness of the field not satisfactory, and in 2 cases it was necessary to supplement arfonad with procainamide. After the drip was stopped it required up to 20 minutes for the blood pressure to return to normal, but this could be accelerated by levelling the table, and in 2 cases was hastened by the injection of methylamphetamine.

Michael Kerr

640. **Cardiovascular Reflexes during Intrathoracic Surgery**

D. L. CRANDELL and J. F. ARTUSIO. *Current Researches in Anesthesia and Analgesia* [*Curr. Res. Anesth.*] **32**, 227–241, July–Aug., 1953. 7 figs., 11 refs.

The authors describe 5 cases in which severe hypotension occurred during thoracic operations at the New York Hospital; in 3 of them, sudden cardiac arrest supervened, one of these patients dying. A description of the sympathetic and parasympathetic nerve supply to the heart and lung is given, and it is suggested that reflex disturbances are more likely to occur in operations on the right side of the chest, because the right vagus nerve supplies the sino-auricular node, whereas the left vagus supplies the auriculo-ventricular node. The thoracotomy was right-sided in 3 of the 5 cases reported. Curare was used for intubation, but not during the operation, in which anaesthesia was maintained with cyclopropane and ether. Measures to prevent or reduce reflex cardiovascular disturbances during thoracic surgery are discussed.

D. D. C. Howat

641. **Prevention of Postoperative Chest Complications**

J. DAVIDSON. *Lancet* [*Lancet*] **1**, 1225–1226, June 20, 1953. 5 refs.

One of the primary causes of chest complications after upper abdominal operations is impairment of respiratory movement due to pain at the site of the incision. This, it is claimed, can be relieved or greatly diminished by intercostal block with benzocaine (2%) and urethane (6%), producing analgesia which may last for 90 days or more. At the end of the operation, before the patient leaves the theatre, an injection of 1 ml. of 2% benzocaine in olive oil followed by 1 ml. of 6% aqueous urethane solution is given in the mid-axillary line on both sides, the needle being left in position while the syringe is changed. The urethane precipitates benzocaine crystals around the nerve, prolonging its action.

Of 76 patients undergoing abdominal operations, all of whom were considered liable to develop postoperative chest complications because of concurrent disease, such complications arose in only 4 (5·3%) after intercostal block had been carried out. There were no complications directly due to the analgesia, but there was one death from a " blown " duodenal stump; the author also points out that there may be a danger that the analgesia will mask pain due to peritoneal irritation.

A. M. Hutton

642. **Continuous Succinylcholine Chloride with Pethidine in Abdominal Surgery**

G. HERINGTON and E. JAMES. *British Medical Journal* [*Brit. med. J.*] **2**, 317–320, Aug. 8, 1953. 1 fig., 10 refs.

The sequence of thiopentone, nitrous oxide and oxygen, and a relaxant has been aptly described as a " pyramid having as its base apnoea, with sides consisting of narcosis, relaxation, and analgesia ". The present authors point out that this technique gives very good operating conditions, but that the use of longer-acting relaxants raises the problem of controlling the duration of relaxation without administration of an antidote. The effects of the antidote may well be more dangerous than the condition for which it is given. On the other hand, if the patient is returned to the ward partially curarized he may become hypoxic and develop pulmonary complications.

The authors have tried succinylcholine chloride, the short-lived but potent action of which suggested that it would be ideal for prolonged relaxation when given by intravenous drip. In a series of 289 abdominal operations a 0·15% solution of succinylcholine in normal saline was used. Analgesia was not adequate in the early cases, so intermittent small doses of pethidine were given as a routine. Except in short, non-emergency operations a cuffed tube was passed by mouth. Operating conditions were excellent. Breathing started again very shortly after the drip ceased and was normal in from 2½ to 13 minutes. Bleeding was moderate, with little tendency to oozing. Recovery was rapid and the postoperative condition good.

A drip apparatus is illustrated which can be controlled by the single-handed anaesthetist who must also manipulate the bag.

W. Stanley Sykes

Radiology

643. **Protection Against X-rays and Therapy of Radiation Sickness with β-Mercaptoethylamine**
Z. M. Bacq, G. Dechamps, P. Fischer, A. Hervé, H. Le Bihan, J. Lecomte, M. Pirotte, and P. Rayet. *Science* [*Science*] **117**, 633–636, June 5, 1953. 2 figs., 20 refs.

A systematic search for compounds protecting against radiation effects led the authors, working at the University of Liège, to concentrate on "cysteamine" (β-mercaptoethylamine). The intraperitoneal injection of 3 mg. of this substance in mice 1 to 3 minutes before irradiation gave nearly complete protection (97% survival) against the usually lethal effect of 700 r, and a dose of 1,300 r was needed to produce the same mortality curve. (Injection ½ to 3 minutes after or 60 minutes before irradiation had no protective effect). In the protected animals the leucocyte count and body weight fell as in the controls group, but recovery began sooner and proceeded more rapidly. Histologically, also, the radiation lesions were similar in both groups, but regeneration was quicker in the treated animals. This action is thought to be due to competition for the free radicals liberated during radiation. Good therapeutic effect was also obtained in human patients with cancer under radiation treatment. One or more intravenous doses of 200 mg. of cysteamine stopped sickness in 24 hours; alternatively, 300 mg. of the salicylate 3 times daily in gelatin capsules was equally effective.

In discussing the action of cysteamine the authors argue that the "competition" theory cannot account for this protective effect when the compound is given after radiation. They suggest that part of the explanation may lie in its effect on the liver; in rats, cysteamine is effective when given after irradiation only if the liver is screened from the radiation by lead. Other actions of the compound include an anti-mitotic effect on tissue cultures. Large doses (up to 1 g. daily) given intravenously to patients with chronic leukaemia gave good results in 4 of 11 cases. The compound is considered to be the best available substance so far for the protection of mammals against the effects of ionizing radiation.

J. Walter

644. **Radiation Treatment of Hemangiomas.** [In English]
J. Thoms and N. Fjeldborg. *Acta radiologica* [*Acta radiol. (Stockh.)*] **40**, 39–53, July, 1953. 6 figs., 38 refs.

This is a review of the late results of the radiation treatment of hemangiomata at the Radium Centre for Jutland, Aarhus, Denmark, 247 patients (with 293 hemangiomata) who were first treated in 1941 having been selected for study. The methods used were: (1) contact radium applications screened with 0·1 mm. of monel metal only; (2) contact *x*-irradiation at 60 kV, with 0·15 mm. of copper equivalent filter; (3) irradiation with softer *x* rays at 26 kV, or Bucky rays at 12 kV, and (4) radium emanation in wax sheets in some cases of capillary naevus. All were treated as out-patients. Capillary naevi were treated with the softest *x* rays or Bucky rays or with radon. The results were not good and radiotherapy is not recommended for these lesions. Of cavernous hemangiomata, 183 superficial lesions were treated with contact radium; the exact dosage is not stated but the treatment was in most cases prolonged. A period of 4 months was allowed to elapse after the first treatment, and subsequent treatments were given at intervals of 4 to 6 months. Deep cavernous and mixed hemangiomata were mostly treated with 60-kV *x* rays.

In assessing the late results of treatment, complete disappearance of the naevus without visible scarring was classified as "excellent", while a depigmented or slightly atrophic scar visible only on close inspection was classified as "good". Of the 182 cases of superficial cavernous haemangioma treated, 146 (80%) came into these categories, less than 5% (8 cases) were totally unaffected by treatment, in 16 cases (8·8%) residual naevus tissue persisted, and undesirable side-effects occurred in the remaining 12 cases (6·6%). These last included telangiectasis and excessive scarring, though some of these naevi had been ulcerated before treatment. The results in the 43 cases of deep cavernous and mixed-type haemangioma treated were very similar, "excellent" or "good" results being obtained in 35 (81%) and only one case failing to respond.

It is pointed out that with the passage of years the initial result may be either improved or marred by subsequent changes in the area.

It is also emphasized that the fact that a few haemangiomata regress spontaneously should not be allowed to delay treatment; the great majority are persistent, and radiosensitivity tends to decrease as the child gets older. Photographs illustrating remarkable results in some severe cases are reproduced. *E. Stanley Lee*

RADIODIAGNOSIS

645. **Localized Thinning and Enlargement of the Cranium with Special Reference to the Middle Fossa**
A. E. Childe. *American Journal of Roentgenology, Radium Therapy and Nuclear Medicine* [*Amer. J. Roentgenol.*] **70**, 1–22, July, 1953. 13 figs., 10 refs.

The author reports 13 cases of localized thinning and enlargement of the cranium and discusses the causes and significance of such radiological findings. The commonest type of change in the author's cases was bulging forward of one middle fossa and elevation of the lesser wing of the sphenoid. In some cases the postero-lateral

margin of the orbit was indistinct, and occasionally there were changes in the sella turcica. In 8 cases the changes were secondary to subdural collections of fluid—a chronic subdural haematoma in one case and a chronic subdural hygroma in the remainder. Cerebral agenesis or atrophy accounted for one case, and in 2 the bony changes were secondary to a cerebral glioma. Intracranial aneurysm and neurofibromatosis accounted for one case each. As would be expected, such *x*-ray changes are mostly found in children or young adults.

L. G. Blair

646. **The Angiographic Configuration of Intracerebral Metastatic Tumors**

S. Ethelberg and K. Vaernet. *Radiology* [*Radiology*] **61**, 39–48, July, 1953. 4 figs., 24 refs.

The authors have carried out 21 successful cerebral angiographic examinations at the City Hospital, Aarhus, Denmark, in cases of cerebral metastasis. In this paper the angiographic appearances in these cases are discussed, and the differential diagnosis from other forms of cerebral tumour is considered.

In most cases the metastasis was solitary. The commonest location was found to be in the parieto-occipital region, in the terminal territory of the major branches of the anterior and middle cerebral arteries.

The vascular pattern within these tumours was usually a uniform, circular, opaque patch up to one inch (25·4 mm.) in diameter, probably due to venular filling. In others there was a circular or semicircular bundle of delicate arteries surrounding an avascular area. The absence of any form of circulation in the tumour was very rare, providing the exposure was made at the optimum time, late in the arterial or early in the venous phase.

Displacement of vessels was seen, but was slight and usually involved only the smaller arteries. The supplying vessel was often identified and in some cases it was slightly enlarged.

Differentiation from meningiomata is not usually difficult. The latter are relatively uncommon in the parieto-occipital region, displace the large cerebral trunks more, and may be supplied partly by branches of the external carotid artery. Malignant gliomata are usually deeply situated and are characterized by irregular, tortuous vessels and arterio-venous fistulae.

D. E. Fletcher

647. **Clinical Findings and Anatomical Changes in the Lungs after Bronchography with "Per-abrodil BR".** (Über klinische Befunde und anatomische Veränderungen der Lungen nach Bronchographie mit Per-Abrodil BR (viskös 60%))

H. W. Weber and B. Löhr. *Fortschritte auf dem Gebiete der Röntgenstrahlen* [*Fortschr. Röntgenstr.*] **79**, 168–179, Aug., 1953. 3 figs., 15 refs.

The results of bronchographic experiments on rats with viscous "per-abrodil" were inconclusive, but in 4 out of 15 operation specimens of the lungs of patients at the University Surgical Clinic, Heidelberg, who had undergone bronchography with viscous per-abrodil, histological examination showed granulomata containing foam- and giant-cells around a substance which had an affinity for stains similar to that of the viscous medium used in the per-abrodil preparation. In all the 4 cases in which these granulomata were found, the contrast medium had penetrated into the peripheral alveoli and bronchioles. It was observed that this usually took place when the contrast medium had been slightly overheated. The granulomata, however, remained clinically symptomless.

The authors conclude that bronchography should not be carried out in cases of acute bronchitis, since the inflamed and oedematous mucous membrane prevents that rapid elimination of the contrast medium which is to be encouraged. They also gained the impression that "pantocaine" (amethocaine), which had been used for previous examination of the bronchi, acted as a bronchial irritant, and they therefore recommend an interval of at least 2 days between an investigation requiring the use of amethocaine and the performance of bronchography.

A. Orley

648. **The Early Diagnosis of Bronchial Carcinoma by means of a Simple Bronchographic Technique.** (Beitrag zur Frühdiagnose des Bronchial-Ca durch einfache Kontrasdarstellung des Bronchialbaums)

E. Liese, W. Mertin, G. Fruhmann, and B. Klun. *Fortschritte auf dem Gebiete der Röntgenstrahlen* [*Fortschr. Röntgenstr.*] **79**, 179–187, Aug., 1953. 9 figs., 25 refs.

The authors assert that 80% of all bronchial tumours arise in the region of the bifurcation of the bronchi and in the primary and secondary bronchi. These they call the "fundamental bronchi", and the bronchographic method which they have devised at the University Medical Clinic, Cologne, for the demonstration of this region they have therefore named "fundamental bronchography" (*Kernschattenbronchographie*).

Having tried various methods of inhalation of a contrast medium for the demonstration of the fundamental bronchi and found them all wanting, they finally adopted an instillation method with an iodized oil. By the use of a special spatula, which is described, it was found sufficient to instil only 5 to 8 ml. of the oil, and practically the whole of this quantity was expectorated within a few days. The single case illustrated clearly shows the method and usefulness of the technique. In their experience with patients, confirmed by trials on themselves, the iodized oil was found to be much less irritating to the tracheal and bronchial mucosa than water-soluble contrast media, and repeated examinations could therefore be carried out without inconvenience to the patient.

A. Orley

649. **Carcinoma of the Middle-lobe Bronchus**

G. B. Locke. *Journal of the Faculty of Radiologists* [*J. Fac. Radiol. (Lond.)*] **5**, 1–18, July, 1953. 20 figs., 21 refs.

The distinguishing features and radiological diagnosis of carcinoma of the middle-lobe bronchus are discussed with reference to a series of 20 cases seen at the Manchester Royal Infirmary during the past 2½ years. The

relevant anatomy and the various radiological appearances seen in collapse and consolidation of the middle lobe are described, and the technique of radiological investigation is detailed. The author has found tomography in the right posterior oblique position useful for showing the middle-lobe bronchus, and he stresses the value of bronchography, an abrupt occlusion in a bronchus of normal calibre being suggestive of intrinsic tumour.

The condition must be distinguished from an encysted interlobar effusion or empyema which, however, has become relatively rare in the author's experience since the introduction of antibiotics. Differentiation from collapse due to tuberculous enlargement of lymph nodes may cause difficulty, but calcification is frequent in these cases and bronchiectasis or a tapering occlusion may be demonstrated by bronchography. *Sydney J. Hinds*

650. **Tuberculous Bronchitis and Bronchiectasis**
G. SIMON. *Journal of the Faculty of Radiologists* [*J. Fac. Radiol.* (*Lond.*)] **5**, 33–41, July, 1953. 19 figs., 4 refs.

There are two distinct manifestations of tuberculous bronchitis, the common type being associated with, and secondary to, gross parenchymal disease, including cavitation, while in the rarer type the endobronchial lesion is the main or sole manifestation. The present paper is concerned only with this latter type.

Endobronchial lesions of the proximal bronchi will often produce obstructive atelectasis or distal bronchiectasis with consolidation, and in such cases tomography is useful for demonstrating the stenosis, which may also be visible through the bronchoscope. Lesions situated more peripherally may give the non-specific radiological appearance of a homogeneous circular shadow 1 to 3 cm. in diameter, in which case tomography is essential and may show features suggesting the nature of the pathology which do not appear on a plain film, such as the " cat's-eyes " (two closely placed circular translucencies within the opacity) or " tennis-racket " appearance. The diagnosis of the condition will influence treatment since it seems to respond best to surgery. A number of typical cases are described, and the paper is illustrated with reproductions of radiographs and photographs of resected specimens.

[This paper merits the attention of anyone interested in diseases of the chest. It derives much of its value from the author's close collaboration with clinician and pathologist.] *Sydney J. Hinds*

651. **Significance of the Buckled Innominate Artery**
E. I. HONIG, W. DUBILIER, and I. STEINBERG. *Annals of Internal Medicine* [*Ann. intern. Med.*] **39**, 74–80, July, 1953. 4 figs., 10 refs.

In this short paper from the New York Hospital–Cornell Medical Centre, the authors discuss the significance of buckling of the innominate artery. This condition occurs in elderly subjects with arteriosclerosis, and is usually associated with an unfolded aorta. On the ordinary postero-anterior chest radiograph a prominence of the right border of the superior mediastinum or a shadow in the right upper zone may be seen, findings which simulate tumour or other conditions. The authors state that although the condition is of little clinical significance, it is important that it should be correctly diagnosed to prevent unnecessary thoracotomy. The diagnosis may be readily established by angiocardiography. *Sydney J. Hinds*

652. **Estimation of the Size of the Chambers of the Heart by Means of Cardiac Catheterization.** (Grössenbestimmungen der Herzhöhlen mit dem Herzkatheter)
A. SCHAEDE and P. THURN. *Fortschritte auf dem Gebiete der Röntgenstrahlen* [*Fortschr. Röntgenstr.*] **79**, 21–32, July, 1953. 10 figs., 5 refs.

An enlargement of the cardiac shadow to the left may be entirely due to an enlarged right ventricle, but in persistent ductus arteriosus and interatrial septal defect the configuration of the heart may be similar although the latter condition overloads only the right ventricle, while the former overloads both ventricles. The two conditions can be differentiated, however, by catheterization of the heart with a radio-opaque catheter. The same method also allows differentiation between mitral stenosis and mitral insufficiency. This is important in view of the benefit to be obtained from operation in cases of pure mitral stenosis and the lack of such benefit in cases of mitral incompetence.

The radiographic differentiation between the two conditions is described in detail. One point in the procedure is particularly stressed: whenever the catheter is used it is essential to direct its tip on to the left wall of the ventricle, thus enabling the size of the ventricle to be estimated. Antero-posterior, oblique, and lateral films are taken, for reasons which are explained. An inadvertent penetration of the tip of the catheter into the coronary sinus can be recognized from measurement of pressure and from gas analysis of the blood withdrawn.

[The thirteen radiographs reproduced, showing the position of the catheter in the various conditions analysed, adequately demonstrate the usefulness of the method.] *A. Orley*

653. **The Clinical Significance of Pharmacoradiography, Particularly with Morphine, in Diseases of the Stomach and Duodenum.** (Die klinische Bedeutung der Pharmakoradiographie, insbesondere des Morphiums, bei Erkrankungen des Magens und des Duodenums)
H. U. STÖSSEL. *Schweizerische medizinische Wochenschrift* [*Schweiz. med. Wschr.*] **83**, 657–660, July 11, 1953. 7 figs., 23 refs.

The earliest radiological sign of a carcinoma of the stomach is localized rigidity, but it is almost impossible to recognize this with certainty if the tone of the stomach is low or if peristalsis is feeble. A number of drugs which stimulate the stomach have been recommended as a means of overcoming this difficulty, but most of them have undesirable side-effects. Much the safest and most reliable is morphine, which was first used for this purpose by French radiologists in 1941. The subcutaneous injection of 0·01 g. of morphine hydrochloride produces maximum activity in 15 to 20 minutes, while if 0·005 g. is given intravenously the effect is almost instantaneous.

After the morphine is injected the patient should lie supine. About 180 to 200 ml. of barium emulsion should be used—smaller amounts do not distend the stomach sufficiently to bring out the effect of the morphine, and if larger amounts are used, or if the patient is left in the erect position, the stomach may not be able to contract against gravity. The indications for the diagnostic use of morphine are: (1) when the body, antrum, or duodenal cap is incompletely filled and the margin of the barium shadow is blurred; (2) when peristalsis is shallow and sluggish and emptying is inefficient; (3) when there are dubious filling defects or niches; (4) in order to see whether an apparently rigid area is really rigid when vigorous peristalsis passes through it; and (5) when it is impossible to locate the pyloric sphincter because its normal anatomy is distorted.

Denys Jennings

654. **Cholecystography. Observations on the Technique of the Examination and the Interpretation of its Results**

I. R. S. GORDON. *Quarterly Journal of Medicine* [*Quart. J. Med.*] **22**, 261–284, July, 1953. 45 refs.

The author reviews the findings in a series of 400 unselected cases undergoing cholecystography at the United Bristol Hospitals. He discusses at length the influence of the technique used, and advocates the use of graded dosage of pheniodol, the dose being determined by body weight. [Since this article appeared another substance, " telepaque ", has come into more general use and may probably have modified the import of the foregoing.]

In discussing the interpretation of the various features of the cholecystogram the author deals with density of shadow, rate of filling, contractility, and visibility of ducts. He then proceeds to the significance of the findings in terms of disease of the gall-bladder, and analyses the results in his own series of cases. In a further series of 90 cases, the author compares the results of cholecystography with the pathological findings as revealed at operation. These are tabulated, and compared with an analysis of various series taken from the literature.

The figures show well over 90% of correct findings when the cholecystograms revealed abnormal gall-bladder form or function, but when the cholecystogram was normal, agreement with the operative findings was reduced to 83% of cases. This figure is in accordance with the known ability of the diseased gall-bladder, in certain circumstances, to concentrate the opaque medium up to a normal density. *A. M. Rackow*

655. **Improved Method for Splenoportography Using Biplane Serialized Exposures**

G. TORI and W. G. SCOTT. *American Journal of Roentgenology, Radium Therapy and Nuclear Medicine* [*Amer. J. Roentgenol.*] **70**, 237–241, Aug., 1953. 1 fig., 15 refs.

The authors, from Washington University, St. Louis, describe a technique for spleno-portography in dogs, which with further refinement may, in their view, have clinical uses. The dog is anaesthetized with pentobarbitone sodium (1 ml. per 5 lb. body weight; 0·45 ml. per kg.). Biplane exposures are obtained, roll-film cassettes with frames measuring 9½ by 9½ inches (24 by 24 cm.) being used. The injection is made directly into the spleen with a needle of 16–18 gauge similar to, but slightly larger than, a lumbar puncture needle. In some cases it was necessary to expose the spleen to give the injection, which consisted of 10 to 20 ml. of " urokon sodium 70 " (sodium aceterizoate, 3-acetylamino-2:4:6-triiodobenzoic acid). Two exposures were obtained before the injection was given. The contrast medium was injected in 2 to 3 seconds and exposures taken continuously at a rate of 2 per second for 6 to 10 seconds. The authors state that there was little evidence of damage to the spleen, beyond some minor subcapsular haemorrhage and a moderate dilatation of the sinusoids. They consider that splenic haemorrhage is a considerable hazard of the procedure, which should be reserved for cases in which the information to be gained will justify the risk.

John H. L. Conway-Hughes

656. **Experimental Method for Visualization of the Hepatic Vein—Venous Hepatography**

G. TORI and W. G. SCOTT. *American Journal of Roentgenology, Radium Therapy and Nuclear Medicine* [*Amer. J. Roentgenol.*] **70**, 242–246, Aug., 1953. 2 figs., 12 refs.

Methods hitherto used for radiological visualization of the liver are discussed, and a new experimental technique which has been tried at Washington University, St. Louis, is described.

In general two techniques have been used: (1) intravenous injection of a radio-opaque chemical in an emulsion, suspension, or oil, which is removed from the blood stream by the liver cells; and (2) injection of an opaque chemical into the vascular tree of the liver. In the first of these, thorium dioxide was tried but had to be abandoned on account of the injurious effects induced by its radioactivity. In 1939 a tri-iodide ethyl ester of stearic acid in colloidal suspension was introduced, but this also was abandoned because of instability of the colloid. During the past year a more stable substance, an aqueous emulsion of ethyl-di-iodostearate (" angiopac ") was tried; it was found that after an intravenous injection of 25 ml. moderate opacification of the liver was produced in 15 to 30 minutes. Experience with angiopac, however, is not yet sufficient to justify recommending it for clinical trial. The use of emulsified radio-opaque oils has hitherto proved unsatisfactory.

Three methods are available for visualization of the vascular system of the liver: (1) injection of the hepatic artery; (2) injection of the portal vein; and (3) retrograde injection of the hepatic vein. The authors state that the first of these methods cannot be relied upon to produce constant visualization of the vessels, and the second, although it has been used in clinical practice, has not yet been perfected.

The authors have devised a technique which so far has been used only on animals. A double-lumen Cournand catheter equipped with a small balloon fitted

round the lateral opening in the end of one of the lumina is introduced into the femoral vein until its tip is 2 to 3 cm. above the diaphragm in the inferior vena cava. A few ml. of opaque medium is introduced into the balloon to make it visible. A second catheter of polythene is then introduced until its tip is 3 to 4 cm. below the balloon, and 3 to 4 ml. of contrast medium is injected into the catheter. The balloon is distended with opaque material and 20 ml. of " urokon 70 " is rapidly injected into the polythene catheter. Biplane exposures are obtained on roll-film cassettes at ½-second intervals for 4 to 5 seconds, when the balloon is deflated to allow the hepatic vein to empty into the inferior vena cava. Excellent visualization of the efferent venous system of the liver is obtained. *John H. L. Conway-Hughes*

657. **Roentgenological Findings in Tuberous Sclerosis. Bone Manifestations**
H. I. BERLAND. *Archives of Neurology and Psychiatry* [*Arch. Neurol. Psychiat. (Chicago)*] **69**, 669–683, June, 1953. 10 figs., 14 refs.

The calcifications of the skull and brain found in tuberous sclerosis are multiple and bilateral. They vary in size and shape and may be within the bones of the calvaria or in the brain.

The osseous changes in the hands and feet are of more significance than was formerly believed. The diagnosis of tuberous sclerosis should always be considered when (1) cyst-like lesions are present in the phalanges; (2) irregular thickening of the cortex of the metatarsal or metacarpal bones is present, or (3) irregular thickening of the cortex of any of the bones of the hands or feet associated with fragmentation or cyst-like changes is present. When these findings present themselves with calcifications within the skull, the diagnosis can be clearly established. The percentage of cases in which both these changes are present can be estimated to be between 60 and 65%.—[Author's summary.]

658. **Venography of the Lower Limb**
G. L. GRYSPEERDT. *British Journal of Radiology* [*Brit. J. Radiol.*] **26**, 329–338, July, 1953. 19 figs., 11 refs.

The author describes a simple method of ascending venography which was devised to show whether the deep veins of the leg are present and patent, if they have demonstrable valves, and also whether incompetent communicating veins are present.

The technique, which has been carried out on 150 cases at St. Thomas's Hospital, London, is as follows. The patient (who should previously have been briefly instructed in the Valsalva manœuvre) lies supine with the foot of the table tilted 15 degrees downward, the limb being rotated a little externally and a pad placed under the heel. The film cassette is placed under the leg to include a field from the malleoli upwards. A small cut is made down to a superficial vein on the dorsum of the foot and a polythene catheter introduced for a distance of 1 cm. up the vein, the tube being then connected with a positive-pressure saline-infusion apparatus controlled by a sphygmomanometer. A test dose of 2 ml. of 35% diodone is injected and normal saline slowly infused. If all is well, 3 minutes later a rubber-tube tourniquet is applied round the lower limb tightly enough to occlude the superficial venous system, and 50 ml. of 35% diodone is injected in 15 seconds. When 10 ml. remains in the syringe the patient is instructed to perform the Valsalva manœuvre smartly and the exposure is made as the syringe is emptied. The Potter–Bucky tray is loaded, the tube column moved to the thigh, the patient repeats the Valsalva manœuvre, and a film of the thigh region is taken 3 seconds later. When these two films have been studied, a third film, centred over the popliteal fossa, is also usually obtained.

The importance of the Valsalva manœuvre in demonstrating the condition of the valves is emphasized, and some of the anatomical variations to be expected are enumerated. The method described is advocated as a primary venographic investigation in cases where venography of the lower limb is clinically indicated. Certain modifications of the technique may be required in particular investigations. *John H. L. Conway-Hughes*

659. **The Practical Uses of Venography**
F. B. COCKETT. *British Journal of Radiology* [*Brit. J. Radiol.*] **26**, 339–345, July, 1953. 14 figs., 5 refs.

The author, writing from St. Thomas's Hospital Medical School, London, points out the important paradox that of the hundreds of patients seen with obvious varicose veins of the great or small saphenous system, very few have ulcers; on the other hand, of those who have ulcers, just under half show no evidence of superficial varicose veins, the majority of these ulcers being due to deep venous incompetence. It is in this latter group that venography is of great practical help in treatment. The valves of the veins are destroyed by thrombosis, which may be confined to the calf or may occur as a deep femoral thrombosis, and may be segmental or in continuity with all the deep veins of the legs. These patients are usually seen 2 or 3 years later with the following triad of symptoms: (1) a heavy aching pain felt in the calf and lower leg, particularly towards the end of the day; (2) swelling of the ankles and leg; and (3) ulceration at the ankle. The Valsalva technique has been of the greatest value in demonstrating these incompetent deep channels. Ligation of the deep veins relieves the pain, but has little effect on the swelling and ulceration.

Above and behind the internal malleolus there are three relatively large and constant perforating veins. The upper one of these has a large communication with the saphenous vein, the lower two, which lie in a straight line behind the great saphenous vein, drain the superficial tissues directly into the deep veins. Incompetence of one or more of these perforating veins is probably the main local factor in the causation of ulcers in this region. These veins can be readily shown by the slow injection (over one minute) of 20 to 25 ml. of 50% " pyelosil " into a small vein on the dorsum of the foot, with the patient erect, the film being taken half a minute after the injection. The upright position is important, as the contrast medium is then held in the region by gravity.
John H. L. Conway-Hughes

History of Medicine

660. **Dupuytren: an Undeserved Reputation.** (Dupuytren: una fama immeritata)
P. FRANCESCHINI. *Rivista di storia delle scienze mediche e naturali* [*Riv. Storia Sci. med. nat.*] **44**, 92–103, Jan.–April, 1953. 7 refs.

In this iconoclastic essay the author examines the career of Baron Dupuytren and concludes that historians have continued to accept this "celebrated" French surgeon at his own valuation without real justification. The many faults in his personal character have long been admitted; in addition, the author cites the numerous achievements of Dupuytren's contemporaries in one of the most brilliant periods of French medicine and shows how Dupuytren, through ignorance or jealousy, did his best to minimize or deny their importance. The most striking examples of this harmful egomania are his treatment of Louyer-Villermay's account of appendicitis (1824), owing to which it is still not appreciated that this work anticipated that of Fitz; and—more important—the extraordinary history of "Lembert's suture". The author states that this epoch-making advance in intestinal surgery was really carried out by Charles Lambert, a pupil of Dupuytren's hated rival, Lisfranc, and reported to the Académie Royale de Médecine on January 26, 1826. Dupuytren later attributed it to his own pupil Antoine Lembert, and said that even Lembert had been anticipated by another of his pupils, Jobert de Lamballe ("both are equally perfect"). In fact, the latter had merely repeated methods used in the 17th and 18th centuries by Palfyn and Ledran and had taken them no farther. (Those who wish to investigate this claim are referred to the author's history of intestinal suture (*Rass. clin.-sci. Ist. biochim*, 1947, **23**, 84).)

[Without accepting all the author's conclusions, it must be admitted that he has presented a strong case for a critical reassessment of Dupuytren's role in the history of surgery.] *F. N. L. Poynter*

661. **Broussais, or a Forgotten Medical Revolution**
E. H. ACKERKNECHT. *Bulletin of the History of Medicine* [*Bull. Hist. Med.*] **27**, 320–343, July–Aug., 1953. Bibliography.

The details of the genesis of the Paris Clinical School, in which modern scientific medicine had its beginnings in the first half of the 19th century, have largely been forgotten. The honour of creating the "Paris movement" should rightly go not to Laënnec, as is generally supposed, but to Broussais, that explosive, aggressive, iconoclastic figure of the Restoration period, whose revolutionary break with the past and new characteristic orientation towards lesion and "localism" (in place of symptoms and "essentialism") marked him as the real creator of "physiological medicine".

From 1803 to 1814 Broussais served as a physician in Napoleon's armies in Europe, and by 1808 had collected enough material from his own clinical observations and from necropsy records to publish his *Histoire des phlegmasies ou inflammations chroniques*, in which he was already stressing gastro-intestinal inflammation as the main cause of death, a thesis which he expanded and brought to a larger public in 1816 in his *Examen de la doctrine médicale généralement adoptée*. This latter book "acted like a bombshell" and marked a turning point in the history of French medicine. It set out to prove that the "essential fevers" of Pinel, as well as most other diseases, were inflammations, especially of the gastro-intestinal tract, and that the treatment should be energetically "antiphlogistic with local bleeding by leeches and a low diet". His oratory and the novelty of his teaching drew such large crowds of students that twice he had to move to larger lecture halls. It was the age of systems, and although Broussais claimed to have made a *tabula rasa* of the teaching of the past and professed to have re-established medicine on new foundations, he was in many ways in line with the Scottish "reformer" John Brown, from whom stemmed his "stimulation theory" of life and disease.

The details of Broussais's life, his successful military career, his political bias, his incessant fights with his opponents, are well described in this paper, which also includes a clear analysis of his system and a concise summary of the 468 propositions which opened the second edition of the *Examen*. Broussais was an extremely logical thinker, but much sophistry was needed to support his thesis that most diseases would either start or end in gastro-enteritis, "the knowledge of which is the key of pathology".

The author states that "the theory of sympathies is long outdated; the monism of gastro-enteritis . . . was never more than a fantasy. Broussais' therapeutics are today repulsive. . . . As a whole the Broussaisian movement strikes us today as belonging to that type of locomotion which has been characterized as 'one step forward, two steps backward'. The main problem for us today seems no longer the intrinsic weakness of this doctrine . . . but the surprising fact that its time fell so enthusiastically in step with it".

To many of his contemporaries Broussais was primarily the proponent of certain general ideas and only secondarily the defender of opinions concerned with details. "We tend today to overlook those general ideas in Broussais because they have become commonplace to us. To his contemporaries they were new, very important, very progressive, and made him very popular". Among such general ideas were his "anti-essentialism and anti-ontology"; his physiological concept of disease and mental processes; his localism, which looked primarily for the tissue lesion rather than the symptom. It was the novelty of these concepts which caused Daremberg to declare in 1870 that they would give to Broussais "l'impérissable titre à occuper une des places les plus élevées dans l'histoire de la médecine". *D. P. McDonald*